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The Subjective Side of Fatigue in Industry

The Carcinogenic Potency of Mineral Oils

Note on the Determination of Small Amounts of Benzene Vapors in Air

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THE JOURNAL OF INDUSTRIAL HYGIENE

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THE SUBJECTIVE SIDE OF FATIGUE IN INDUSTRY*

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THE increased tempo of modern industry has caused the problem of fatigue to become more and more important from a purely management standpoint. Formerly, though hours were long, the individual workman was given a certain freedom inside the plant and was expected to adjust his rate of production in such a way as to compensate for the drain of his work. The modern theory expects the worker to produce at full speed all the time he is in the plant. If he is caught resting on the job, that is usually sufficient cause for a reprimand from the foreman. This change in policy makes management responsible for the proper adjustment of the requirements of the job to the capacity of the worker.

A satisfactory solution of this problem has not yet been found, though many worth-while and helpful attempts have been made. These efforts may be placed in four categories: (1) the lessening of the energy involved in the work itself, as in the Gilbreth idea of motion study to eliminate useless movements, and the increased use of machinery; (2) better utilization of the time spent on the job, as illustrated by the inauguration of authorized rest periods; (3) a lessening of the total time spent in the plant, as seen in the movement for the six-hour day and the five-day week; and (4) the search for definite, objective and easily applied methods of determining when a worker is unduly fatigued, as, for instance, by reaction tests, analysis of the carbon dioxide content of the exhalation, and blood pressure readings, in order to see whether efforts to lighten the tension of the job are necessary or not. Some of the methods just mentioned, such as the five-day week, may also, it is true, serve other purposes, but there can be no doubt that one of their main

* Received for publication Feb. 26, 1931.

functions is to reduce the tension of the job.

A final solution of this perplexing problem depends without doubt upon our ability, sooner or later, to work out scientific methods of measuring fatigue, methods simple enough, however, to apply readily in the shop. In spite of all these efforts, there is one field of investigation which has been almost entirely neglected. That is the study of the workers' feelings of fatigue, or, in other words, the subjective side of fatigue in industry.

The chief difficulty facing one in such a study is the indefiniteness of the feeling. It is very difficult to make sure that when two workers say they are tired, they both mean the same thing. Likewise, how can the same person express accurately the varying intensity of the feeling at one time as contrasted with another. On the other hand, the feeling of tiredness is really just as important as so-called fatigue; for fatigue is not a conscious element in one's mind unless one feels tired. Moreover, just because a problem is difficult is no reason why it should not be tackled. It must only be remembered that the conclusions are to be looked upon more as suggestions than as laws.

It was with all these considerations in mind that the analysis of the feeling of fatigue was included as part of a much broader study involving the relation of workers to their total situation.

A large public utility corporation in the East invited the writer, under the auspices of the Department of Industrial Research of the University of Pennsylvania, to devote a whole year to the observation of a group of normal workers of various occupations, ages, personality types, and nationalities. They were studied carefully in regard to (1) overt behavior, such as efficiency, lateness, co-operativeness, verbal outbursts, constructive ideas, and absenteeism; (2) emotional behavior; (3) dominant trends of thought and reverie; and (4) such physical and physiologic items as could be either detected or measured, such as blood pressure, chylomicron content of the blood, weight, hours of sleep, illnesses or pains, and feelings of fatigue. Special emphasis was laid on the analysis of relationships existing between these items and environmental conditions or personality traits.

The observer spent all of the working day in almost constant contact with the workers studied, and much of the time after work with them, either in their homes or elsewhere, endeavoring thereby to obtain a complete picture of their whole life. All of them had full knowledge of the purpose of the study and co-operated fully both in describing and in analyzing their behavior. Twelve men were followed throughout the year and five others were studied with the same care for periods of several months. In addition to these seventeen, over a hundred workers were included at one time or another in some phase of the fatigue study. It is hoped that the results of this work may prove of interest not only to employers, but also to the many who desire to understand and control their own feelings of tiredness.

"My! but I feel tired this afternoon. Will that darned whistle never blow?" How often does one hear some expression like that? When does a man feel

tired? What are the causes? Does the tired feeling coincide with true fatigue?

We find that a man may feel tired at any time, apparently without "rhyme or reason." He may be tired when he comes to work in the morning, a feeling which usually passes away sometime during the day. Right after lunch he sometimes feels both drowsy and tired. Sometimes he is worn out, tired or "a little tired" in the hour before quitting time. Sometimes he feels fine throughout the working day, but as soon as he gets home and bathes, the tired feeling strikes him and all he wants to do is sit in an easy chair, read the paper, and then go to bed. Or, in an hour or two after he gets home, he may have aroused enough enthusiasm to be all ready for a show, card party, or "some excitement."

Can it be taken for granted when such a person says he feels tired, that he is really fatigued? For fatigue, let us accept the definition agreed upon by the British Committee on the Health of Munition Workers: "Fatigue is the sum of the results of activity which show themselves in a diminished capacity for doing work."[1] However, the feeling of fatigue may not coincide with a lowered rate or amount of actual work accomplished during the period that the worker feels tired; for sometimes more work was turned out during a morning or afternoon when the worker felt tired, than during a similar period when he was feeling fine. This reaction is not the rule, but one cannot get away from the fact that it does occur. The problem is further complicated by the fact that there seem to be cumulative effects of activity under certain conditions, if not of all activity, which cannot be foretold by the lowering of capacity for work or by any other definite test, but which seem to explode somewhat like a bomb and require a vacation or a new job.

Take the case of James K., a young man of 24, who worked steadily twenty hours a day for a period of ten days without noting at the time any particular symptoms of fatigue. The day after he returned to his usual schedule a definite listlessness and a nervous inability to remain steadily at any one task became evident. Six months passed before he had completely recovered.

William G. worked very consistently for five and one-half months, without taking any recreation or physical exercise. After the completion of that particular piece of work he was unable to continue with his job for six weeks. His systolic blood pressure, taken in the standing position, showed a drop of almost 15 points. Workers very frequently show minor instances of a similar nature, when they let down for a day and do just as little work as they possibly can, after they have completed a day or two of very strenuous effort.

If fatigue and the feeling of tiredness coincided at all times, one of our most serious problems, both industrial and purely personal, would disappear. In understanding the reasons for the discrepancy, the first point to keep in mind is that energy is stored in different parts of the body, in the blood,

[1]Industrial Health and Efficiency. Health of Munition Workers Committee, Final Report, p. 15. London, H. M. Stationery Office, 1918.

glands, nerves, muscles, and fatty tissue. The most available supply of energy is that in the blood stream. The supply in the muscles, nerves, and glands is almost as readily available but seems to vary more with the nature of the stimuli calling it forth. The rest of the stored body energy is still more remote. Almost every part of the body represents energy in some form and in times of great stress can be used. Thus we have the origin of the saying, "wasted away to skin and bones."

It is as much a function of the body to create more energy as it is to consume that already created. When this is being done the anabolic machinery is functioning and is using up a certain amount of energy in making more available. While this process of storage is taking place, other things being equal, the catabolic machinery, which expends energy, displays a natural tendency to slow down. If there is no exciting demand for activity focusing on the outer world, the energy available may not even be sufficient for keeping awake, and a feeling of drowsiness results. As more sources are tapped or as the lunch is digested, more energy is made available and the feeling wears off.

We observe the same type of reaction in "warming up." The worker often feels tired the first half hour or more after he arrives, but strikes a proper balance after he gets "sweated up." If he got too little sleep the night before or drank too much, the proper balance may not be attained until the late afternoon.

Once the worker gets into the swing of the work, he hates to stop, because he "gets tired." A short stop seems to be of some benefit, possibly more mentally than physically, but an enforced break of more than ten or fifteen minutes, especially if he cannot relax fully or sit down comfortably, seems to throw him out of the swing of the work both mentally and physically. Those workers who could lie down and completely relax, possibly getting just to the point where they "hit the bed," as I have heard it expressed, did not feel the slowing down effects of the average stoppage of work, where bodily tension was maintained. It is likely that such a complete rest period, to achieve the best results, should occur just before the tired feeling is about to begin, and the length of the period of relaxation should vary with the person's nervous make-up and physical state. If the rest develops into a nap of some duration, the worker's feelings are usually worse than before the nap, and his difficulty in reestablishing the "working ratio" is very noticeable. It is likely that the short rest gives the vital organs a chance to recoup but not to turn anabolic with reference to the body as a whole.

The feeling of tiredness may be expressed in a mathematical relationship:

$$\left.\frac{\text{Amount of energy available at the moment}}{\text{Amount of energy demanded at the moment}}\right\} =$$

Feeling of pleasure in the activity
or
Feeling of fatigue

If this fraction results in a whole number or more, then the feeling is one of bodily well-being; if the result is a proper fraction, a feeling of tiredness is produced.

How will this theory explain other cases of tiredness? Distasteful or disgusting work brings on the feeling quickly. In both cases the worker's mental and emotional state is negative, the glands or other secondary sources of energy are not easily tapped, and the ratio is less than one. The same is true of the man who "gets more tired at home doing nothing than when he is working." His body may even be building up its store of energy during the rest, but the stimulus of just living does not render available sufficient energy even to keep him happily awake.

A similar condition exists with boredom. In an upholstery mill, three kinds of material are handled in the winding department. The handling is identical except for the difference in the material—wool, cotton, and silk. The wool is almost constantly breaking and the operatives must be continuously on their feet and active. As a rule, they feel tired before quitting time, a feeling which does not disappear until they have rested a while after supper—sometimes not even then. The cotton keeps the workers fairly active and attentive, but provides brief intervals now and then for a let-down, not long enough, however, to permit them to get out of the swing of the work. If the feeling of tiredness occurs, it is not particularly due to the conditions of the work in this case. The silk breaks or twists very rarely. The workers may sit for as long as fifteen minutes with their eyes idly wandering up and down the spindles. This operation develops boredom and a definite feeling of either restlessness or fatigue, depending upon the temperament and physical condition of the worker. The restless feeling always vanishes with the whistle; sometimes the tired feeling does, but often it hangs on as persistently as when the wool is being wound.

There can be little doubt that the feeling of tiredness caused by wool winding is indicative of true fatigue. In the case of the silk, one would be inclined to think that the worker was merely bored, and would lose his tired feeling with the pleasure of quitting. The workers themselves often remarked that they could not understand why they felt tired, because they "hadn't done anything today." The anomaly is readily explained when we understand the functioning of the glands, especially the adrenal. Cannon has shown that strong emotion causes these glands to function and to throw their products directly into the blood stream, thereby increasing the "energy available at the moment." In so functioning they are creating new energy as well as making available stored energy.

Boredom denotes a complete lack of emotion in relation to the work. Therefore not only is energy, however little, being consumed by the workers' merely keeping on the job, but at the same time the stimulation of interest in the work fails to cause fresh energy to be created. *Sustained boredom* should therefore lead to true *fatigue*, unless the workers are unusually "peppy." Then the reaction should be restlessness, because of the desire to work off surplus energy.

Boredom and a feeling of tiredness are thus often the result of a mental attitude. Does this conclusion mean that one should never feel tired? Hardly. To feel tired is biologically as useful as

to feel hungry. It is about the only symptom of true fatigue we can easily recognize, inadequate and often misleading though it be.

The important question, therefore, is: How much is too much? In taking the average occurrence of the feeling of tiredness in the lives of the healthy, normal workers studied for the period of a year, and contrasting it with the feeling in the cases of those who were clearly under too heavy a strain or were about to experience a breakdown, we may say that normally a person should not *feel tired* for more than a *fifth of his total waking state*. The distribution of the states of tiredness should also not be evenly placed on each day. For instance, one should not wake up tired each morning. Nor should each week contain the same number of tired occasions.

It would seem that there should be a week or more with almost no feeling of fatigue. Then may come a week or more with a greater number of fatigue periods scattered through, after which may come a week or several days when the tendency to feel fatigued on the slightest provocation is very great. Then this sort of cyclical fluctuation should repeat itself. In youth it is likely that the feeling of fatigue should occur even more seldom. But on the whole, that person who practically never feels tired may consider himself fortunate. If, however, the feeling is spaced irregularly during the day and over longer periods, and is normal in amount, *i. e.*, not over 20 per cent. as a long-run average, it may be considered healthy; otherwise steps should be taken to find out what is wrong.

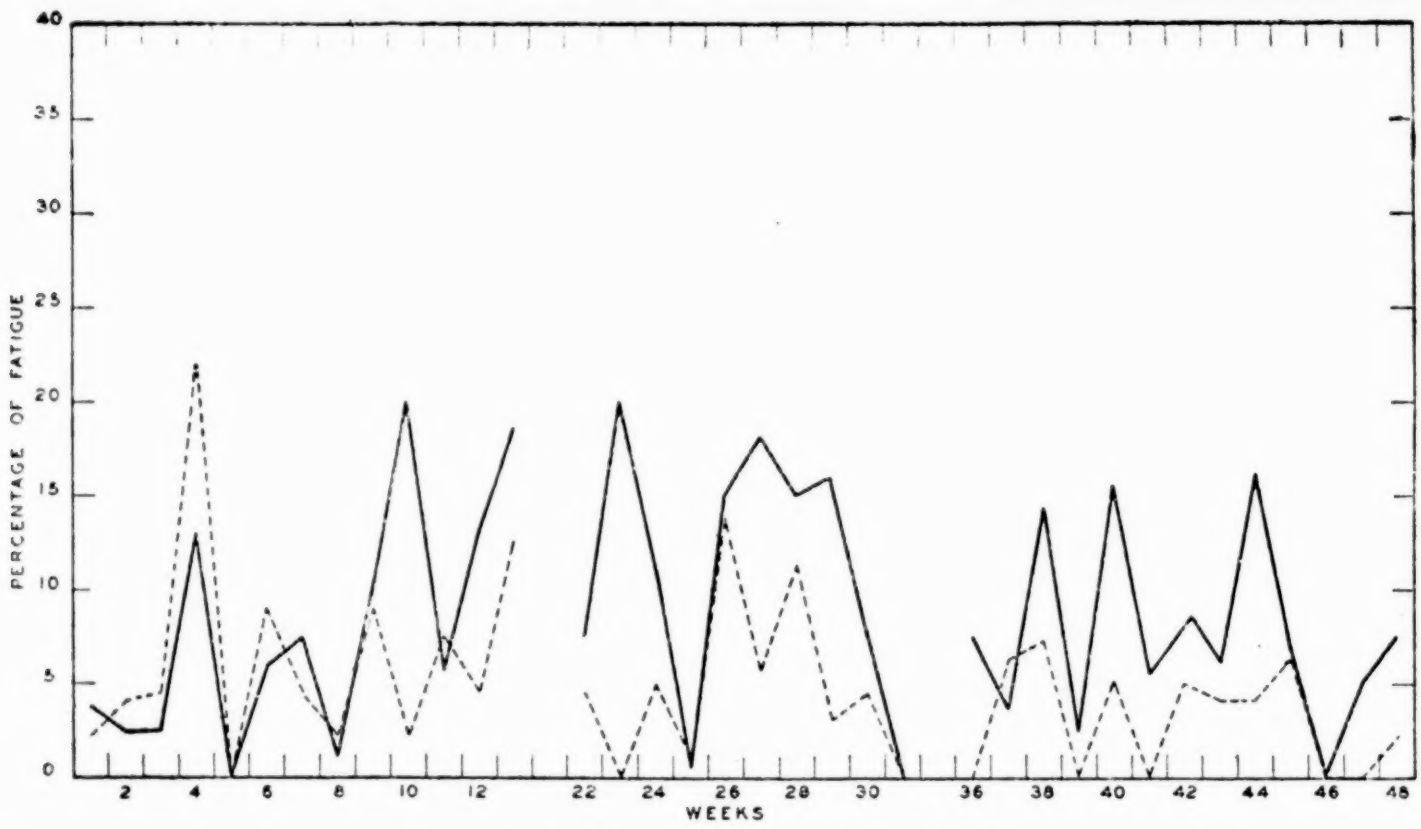

FIG. 1.—Fatigue curves of Worker L.
Broken line = plant fatigue; solid line = total fatigue.

Figures 1 and 2 illustrate graphically the contrast between what would seem to be a healthy amount of tiredness and too much. In both figures the weeks during which Workers L and H were studied are numbered along the bottom from left to right, while the scale on the left-hand margin of the charts shows the average weekly

percentage of tiredness. No observations were made from the thirteenth to the twenty-second week and from the thirty-first to the thirty-sixth week, in order to prevent the study from becoming too boresome to the workers. The term, plant fatigue, includes only the tiredness experienced by the workers during time spent in the plant. Total fatigue shows the percentage of tiredness felt both inside and outside the plant. In order to weight the

Worker L's graph shows a curve of fatigue that is healthy in both amount and variation. His high weeks might go even higher without exciting apprehension. Worker H's graph is also within normal limits for the first twenty-five weeks of the study, in spite of the unusual peak during the tenth week. This high peak is the result of a birth in the family which occurred some four weeks before and placed him under a heavy strain,

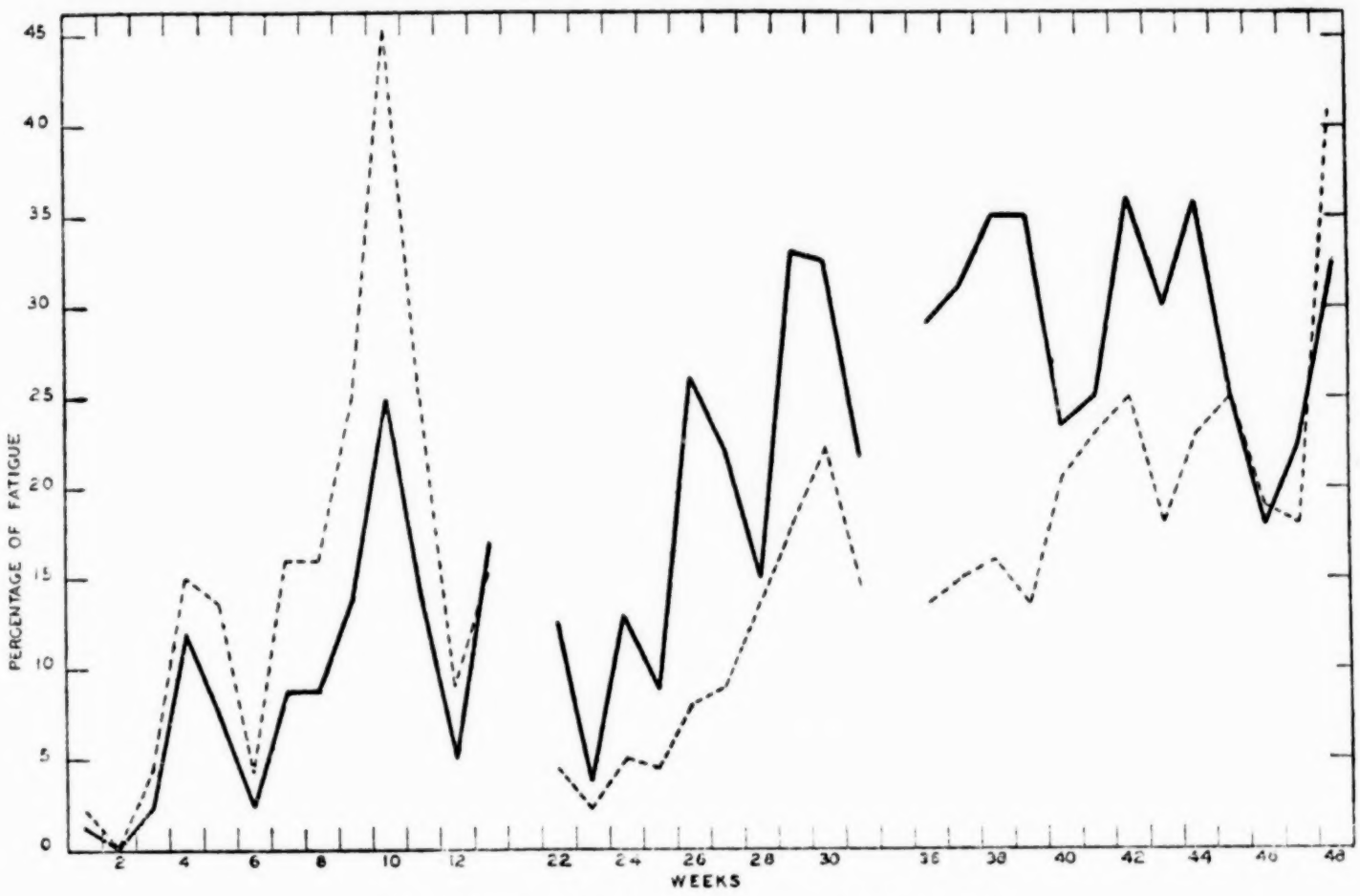

FIG. 2.—Fatigue curves of Worker H.
Broken line = plant fatigue; solid line = total fatigue.

differing degrees of tiredness expressed by the workers, the following scale was used in preparing not only Figures 1 and 2, but also Table 1.

One period,[2] "tired"	= 1 period
One period, "somewhat tired"	= $\frac{1}{2}$ "
One period, "sleepy"	= $\frac{1}{2}$ "
One period, "lazy"	= $\frac{1}{2}$ "
One period, "not exactly tired"	= $\frac{1}{4}$ "
One period, colds, etc.	= $\frac{1}{2}$ "

[2] A "period" is composed of approximately $2\frac{1}{4}$ hours.

besides disturbing his habits of sleep. It is interesting to note how delayed its greatest effect is.

Beginning with the twenty-fourth week H was faced with several crises both at home and in the plant, which were noticeably damaging his physical health and apparently would have led to a definite breakdown had they not been removed. We still notice the fluctuations, but the total amount of tiredness is far above the danger line. His sleep curve also showed a gradual

decline from the forty-first week on, indicating how difficult it was for him to get the proper rest.

Many factors are recognized as being likely to cause both the feeling of tiredness and the true fatigue which usually, though not always, coincides with it. Physical movement or activity, or activity of the senses and their chief nervous organ, the brain, will cause fatigue. The mere maintaining of bodily tension, particularly standing or sitting uncomfortably, which Dr. A. V. Hill, of London University, calls "the general wear and tear on the body," may be a cause. The destructive emotions, such as worry, disgust, fear, and anger, are causes. The struggle to overcome the difficulties of poor lighting, improper ventilation, damp, hard floors, unhealthy toilet facilities, and the lack of properly prepared and nourishing food are common causes. The demands of home, recreation, and other activities often cause a man to come to work without sufficient rest or sleep. Malnutrition and improper elimination and many miscellaneous, but less common causes, such as the use of drugs, pessimistic daydreaming, ill health, particularly colds or focal infections, night work and climatic conditions, may be involved. Boredom or too little activity, glandular malfunctioning, too much vacation or too much sleep, and unsuccessful effort may temporarily, at least, cause a feeling of tiredness which usually does not imply true fatigue.

How these various causes made the twelve workers studied throughout the year feel tired is shown in Table 1. These general causes were worked out through the joint analysis of the workers themselves and the investigator. They represent what seems most likely to have caused the feeling of fatigue at the particular time when it occurred. It will be noticed that the very first item in the table is a question mark. This represents times when the worker was fatigued seemingly for no obvious reason. The total under this heading may seem to be unduly high and perhaps it is; but unfortunately life is not always like an open book. My own analysis of the majority of these instances would lead me to assign them to two general reasons: (1) the delayed or long-continued influence of the more obvious causes already mentioned; (2) malfunctioning of the organism itself, which was not noticeable but was sufficient, in conjunction with the ennui of the daily task or the wear and tear of just standing around, to make the worker feel tired. It is interesting to note that the majority of these instances, where no obvious reason was evident, coincided with a state of low emotional vigor on the part of the worker.

The difficulties involved in working up this table brought out clearly the complexities of the problem of human behavior. To assign the feeling of fatigue to a single cause was usually impossible. Far more often combinations of causes were clearly evident. The following illustration, taken from Worker G's record, will illustrate how the nature of the combinations and their relative strength in each worker's life can be understood from Table 1. Each major set of causes is assigned a number or letter, physical activity or movement being 1, mental activity 2, etc. In G's case, physical activity

alone was responsible for his being tired a total of eight periods during the year, this total being computed as in the weekly percentages (see scale page 191). It is thus listed as 8.0 –1, under its proper heading in the table. The combination of physical and mental activity caused Worker G to feel tired 12.25 periods. This amount is then listed twice thus, 12.25 –1, 2; once under physical activity and again under mental activity. This method was followed for all the other combinations of causes. Thus, one can see not only what the most important single causes of fatigue were in the case of each worker, but also the relative frequency and importance of the various combinations.

The objection may be raised that such a method gives undue weight to the causes occurring in combination, since they are listed at full value under each cause in the combination; whereas the single causes are listed only once. Either the combinations should be broken into their constituent parts and each cause assigned its relative value, or else the periods governed by the single causes should be multiplied by the usual number of causes found in combination. Such an objection would be valid if the purpose of Table 1 were to weigh by statistical methods the importance of the various causes in the case of each worker. That is not its chief purpose. It is intended rather to give an actual picture of the way the various causes seem to operate.

Table 2, on the other hand, does attempt to contrast the relative importance of each of the causes of fatigue for the group as a whole. In this table, three contrasting methods are used. First, the totals are taken from Table 1 without any effort at changing or weighting. Second, all those single items or causes which seemed to be entirely responsible for the feeling of fatigue at the time are totaled for the group, the combinations of causes being left entirely out of the picture. Finally, the method of weighting the single causes through multiplying them by 2 (the usual number of causes found in combination) is utilized.

All these methods find the outside activities the most important single item causing fatigue. Table 1, picturing the causes for the individual workers, shows that Workers G, F, and 1 are exceptions to this rule; but a weighting of the single causes would leave only Worker F as an exception. This conclusion is in keeping with our common sense knowledge of the importance of sleep. One would further expect such a result because that heading had to include a larger number of separate items than the others, such as sleep, parties, family duties of one kind or another.

If we attempt to work out a rough estimate of how important in fatigue causation *all* the non-plant factors were as contrasted with those inside the plant, a fair *estimate* might be as shown in Table 3. In this tabulation, those periods when fatigue seemed definitely caused by physical activity, wear and tear, and physical environment outside the plant, were credited to outside factors. The emotional causes, and malnutrition and colds, were divided equally between the two, as such a division seemed fair from the original data. Climate was credited to outside sources, though it was

TABLE 1.—THE CAUSES OF TIREDNESS

NO OBVIOUS REASON	PHYSICAL ACTIVITY	MENTAL ACTIVITY	BODILY TENSION OR WEAR AND TEAR	EMOTIONAL TENSION	PHYSICAL ENVIRONMENT	OUTSIDE ACTIVITIES INCLUDING SLEEP	MALNUTRITION AND IMPROPER ELIMINATION	COLDS, ETC.	CLIMATE	BOREDOM OR TOO LITTLE ACTIVITY	GLANDULAR MALFUNCTIONING	VACATION OR TOO MUCH SLEEP	UNSUCCESSFUL EFFORT
?	1	2	3	4	5	6	7	8	9	a	b	c	d
					Worker G								
19.50	8.00–1 12.25–1, 2 2.00–1, 3 2.00–1 1.00–1, 2, 4 2.00–1, 6 2.50–1, 9 2.00–c, 1 31.75	12.25–1, 2 1.50–2, 4 1.00–1, 2, 4 14.75	20.50–3 2.00–1, 3 0.50–4, 3 1.00–6, 3 24.00	0.50–4 0.50–4, 3 1.50–2, 4 1.00–1, 2, 4 3.50	0.5–5	23.75–6 1.00–6, 9 1.00–6, 3 2.00–1, 6 27.75	5.50–7	3.75–8	4.50–9 1.00–6, 9 2.50–1, 9 8.00	4.50–a	1.00–b	1.50–c 2.00–c, 1 3.50	.....
					Worker L								
23.00	5.50–1 5.50–1, 2 0.50–1, 4 1.00–1, 6 12.50	0.50–2 5.50–1, 2 6.00	18.50–3 1.00–6, 3 19.50	6.00–4 0.50–4, 1 4.50–4, 6 11.00	4.0–5	18.25–6 4.50–6, 4 1.00–6, 1 1.00–6, 3 24.75	7.00–7	4.75–8	9.00–9	12.25–a	.....	.....	.....
					Worker H								
29.25	6.50–1 19.50–1, 2 10.50–1, 2, 6 3.50–1, 4 3.50–1, 9 5.00–1, 8 3.00–a, 1 3.00–1, 4, 6 54.50	0.50–2 19.50–1, 2 10.50–1, 2, 6 30.50	17.50–3 1.50–3, 9 6.50–3, 4 25.50	12.50–4 3.50–1, 4 2.50–8, 4 1.00–9, 4 15.00–6, 4 4.50–a, 4 6.50–3, 4 3.00–1, 4, 6 48.50	3.5–5	56.75–6 10.50–1, 2, 6 2.00–7, 6 15.00–4, 6 0.75–9, 6 10.50–a, 6 3.00–1, 4, 6 98.50	16.50–7 2.00–6, 7 0.75–d, 7 19.25	0.50–8 2.50–4, 8 5.00–1, 8 8.00	6.00–9 3.50–1, 9 1.00–4, 9 1.50–3, 9 0.75–6, 9 12.75	8.50–a 4.50–a, 4 3.00–a, 1 10.50–a, 6 26.50	0.50–b	.....	0.75–d, 7

Worker X

38.50	3.00–1 10.50–1, 2 2.00–1, 4 1.00–1, 6 1.00–1, 2, 4 2.25–1, 3 3.25–1, 2, 6 23.00	10.50–1, 2 1.00–1, 2, 4 3.75–4, 2 3.25–1, 2, 6 18.50	14.00–3 3.50–6, 3 3.25–d, 3 2.25–1, 3 5.25–4, 3 28.25	15.00–4 2.00–1, 4 1.00–1, 2, 4 5.25–3, 4 16.25–6, 4 3.75–2, 4 2.50–7, 4 45.75	.....	55.00–6 1.50–6, 7, a 1.00–1, 6 3.50–6, 9 3.50–3, 6 16.25–6, 4 3.50–6, d 3.25–1, 2, 6 87.50	6.00–7 1.50–6, 7, a 2.50–4, 7 10.00	.....	2.00–9 3.50–9, 6 5.50	1.50–6, 7, a	.....	2.50–c	2.50–d 3.25–3, d 3.50–6, d 9.25

Worker F

11.50	8.25–1 39.00–1, 2 14.50–1, 2, 4 1.50–1, 2, 8 1.50–1, 2, c 0.50–1, 2, 6 2.00–1, 2, d 1.00–1, 7 2.00–1, 9 5.00–1, 4 1.25–1, a 76.50	1.25–2 39.00–1, 2 14.50–1, 2, 4 1.50–1, 2, 8 1.50–1, 2, c 0.50–1, 2, 6 2.00–1, 2, d 2.00–6, 2 62.25	17.50–3 1.00–3, 4 18.50	14.50–1, 2, 4 5.00–1, 4 1.00–3, 4 4.75–6, 4 25.25	.....	9.50–6 0.50–1, 2, 6 4.75–6, 4 5.50–7, 6 1.75–6, a 2.00–6, 2 24.00	9.75–7 1.00–1, 7 5.50–7, 6 16.25	5.00–8 1.50–1, 2, 8 6.50	3.00–9 2.00–1, 9 5.00	6.75–a 1.75–6, a 1.25–1, a 9.75	.....	1.50–1, 2, c	3.00–d 2.00–1, 2, d 5.00

Worker M

14.75	2.00–1 6.50–1, 2 2.00–1, 2, 9 1.00–1, 2, 4 5.00–1, 2, 6 3.50–1, 5 5.00–1, 4 2.00–1, 6 27.00	6.50–1, 2 2.00–1, 2, 9 1.00–1, 2, 4 5.00–1, 2, 6 14.50	1.00–3 2.50–6, 3 3.50	4.50–4 1.00–1, 2, 4 8.25–4, 6 5 25–4, 9 5.00–1, 4 1.25–4, a 25.25	3.50–1, 5	20.00–6 5.00–1, 2, 6 8.25–4, 6 2.00–1, 6 2.50–6, d 2.50–6, 3 40.25	4.00–7	.....	5.75–9 2.00–1, 2, 9 5.25–4, 9 1.50–9, a 14.50	0.25–a 1.50–9, a 1.25–4, a 3.00	.....	0.50–c	2.50–6, d

TABLE 1.—*Concluded*

NO OBVIOUS REASON	PHYSICAL ACTIVITY	MENTAL ACTIVITY	BODILY TENSION OR WEAR AND TEAR	EMOTIONAL TENSION	PHYSICAL ENVIRONMENT	OUTSIDE ACTIVITIES INCLUDING SLEEP	MALNUTRITION AND IMPROPER ELIMINATION	COLDS, ETC.	CLIMATE	BOREDOM OR TOO LITTLE ACTIVITY	GLANDULAR MALFUNCTIONING	VACATION OR TOO MUCH SLEEP	UNSUCCESSFUL EFFORT
?	1	2	3	4	5	6	7	8	9	a	b	c	d
						Worker Y							
8.25	6.50–1 5.50–1, 2 2.00–1, 4 1.00–1, 2, 9 15.00	5.50–1, 2 1.00–1, 2, 9 6.50	3.00–3, 6	4.00–4 4.00–6, 4 2.00–1, 4 0.50–7, 4 10.50	4.00–5	32.75–6 3.00–6, 3 1.50–6, a 4.00–6, 4 0.50–6, d 1.00–6, 9 42.75	1.00–7 0.50–7, 4 1.50	2.00–8	1.00–9 1.00–9, 6 1.00–1, 2, 9 3.00	1.75–a 1.50–6, a 3.25	.....	7.00–c	2.00–d 0.50–6, d 2.50
						Worker S							
9.75	9.00–1 1.50–1, 2 0.50–1, 6 11.00	1.50–1, 2	2.50–3 1.00–3, d 3.50	2.00–4 1.00–4, a 3.00	.....	34.50–6 0.50–1, 6 2.00–6, a 3.50–6, 8 40.50	4.00–7	3.50–8 3.50–6, 8 7.00	1.50–9, a	2.00–a 1.00–4, a 2.00–6, a 1.50–9, a 6.50	.....	.....	3.00–d 1.00–3, d 4.00
						Worker 1							
30.75	10.50–1 8.50–1, 2 16.50–1, 2, 4 28.00–1, 2, 6 2.25–1, 7 2.00–1, 9 2.75–1, 4, 8 0.50–1, 8 3.00–1, d 74.00	8.50–1, 2 16.50–1, 2, 4 28.00–1, 2, 6 53.00	6.50–3 1.50–4, 3 0.50–3, 5 2.50–6, 3 11.00	21.75–4 16.50–1, 2, 4 2.75–1, 4, 8 1.50–4, 3 3.00–8, 4 4.00–6, 5, 4 3.50–4, 6 2.50–5, 4 6.00–4, d 61.50	21.50–5 0.50–3, 5 4.00–6, 5, 4 2.50–5, 4 28.50	18.75–6 28.00–1, 2, 6 4.00–a, 6 1.00–6, 9 8.00–6, d 1.50–8, 6 4.00–6, 5, 4 3.50–6, 4 2.50–6, 3 71.25	0.25–7 2.25–1, 7 2.50	13.75–8 2.75–1, 4, 8 7.00–8, d 3.00–8, 4 1.50–8, 6 0.50–1, 8 28.50	3.00–9 1.00–6, 9 2.00–1, 9 2.00–9, d 8.00	4.00–a, 6	.....	3.75–c	6.00–4, d 2.00–9, d 8.00–6, d 3.00–1, d 7.00–8, d 26.00

Worker 2

31.00	12.00–1 1.00–1, 4 7.50–1, 6 6.50–1, d 4.00–1, 2 2.00–1, 5 33.00	4.00–1, 2	5.50–3 2.50–6, 3 8.00	9.00–4 1.00–1, 4 6.50–4, d 7.00–6, 4 2.75–c, 4 26.25	16.25–5 2.00–1, 5 18.25	60.75–6 2.50–6, 3 7.50–1, 6 4.00–6, d 7.00–6, 4 81.75	.....	26.00–8	2.00–9, d	5.50–a	.....	5.50–c 2.75–c, 4 8.25	7.00–d 6.50–4, d 6.50–1, d 2.00–9, d 4.00–6, d 26.00

Worker 3

4.50	10.50–1 11.50–1, 2 4.25–1, 4 3.00–1, 9 6.50–1, 6 1.00–1, 2, 4 36.75	11.50–1, 2 2.00–2, 4 1.00–1, 2, 4 14.50	13.00–3 1.00–3, d 2.50–3, 6 16.50	7.00–4 4.25–1, 4 2.00–2, 4 3.50–4, d 34.00–6, 4 4.75–7, 4 3.00–8, 4 1.00–1, 2, 4 59.50	.....	13.75–6 34.00–6, 4 6.50–1, 6 3.00–6, 7, 8 2.50–3, 6 59.75	1.00–7 4.75–7, 4 3.00–6, 7, 8 8.75	22.75–8 3.00–4, 8 3.00–6, 7, 8 28.75	2.00–9 3.00–1, 9 5.00	.....	.....	1.00–c	3.50–4, d 1.00–3, d 4.50

Worker 4

11.25	6.00–1 6.75–1, 4 2.00–1, 4, 6 2.00–1, d 9.00–1, 6 8.50–1, 2 34.25	0.50–2 8.50–1, 2 9.00	3.50–3 2.50–6, 3 6.00	5.50–4 6.75–1, 4 2.00–1, 4, 6 5.25–4, 6 1.25–4, 5 2.00–4, d 22.75	3.00–5 1.25–4, 5 4.25	38.00–6 3.50–6, a 2.00–1, 4, 6 2.50–6, 3 9.00–1, 6 5.25–4, 6 60.25	.....	1.75–8	.....	3.50–a, 6	.....	.....	2.00–1, d 2.00–4, d 4.00

TABLE 2.—RELATIVE IMPORTANCE OF CAUSES OF FATIGUE FOR ENTIRE GROUP OF WORKERS

UNWEIGHTED METHOD		SINGLE CAUSES METHOD		WEIGHTED METHOD	
(6) Outside activities	659.00	(6) Outside activities	381.75	(6) Outside activities	1,040.75
(1) Physical activity	429.25	(3) Bodily tension	120.00	(1) Physical activity	517.00
(4) Emotional tension	342.75	(4) Emotional tension	87.75	(4) Emotional tension	430.50
(2) Mental activity	235.00	(1) Physical activity	87.75	(3) Bodily tension	287.25
(3) Bodily tension	167.25	(8) Colds, etc	83.75	(2) Mental activity	237.75
(8) Colds, etc	117.00	(7) Malnutrition	55.00	(8) Colds, etc	200.75
(d) Unsuccessful effort	84.50	(5) Physical environment	52.75	(7) Malnutrition	133.75
(a) Boredom	80.25	(a) Boredom	41.50	(a) Boredom	121.75
(7) Malnutrition	78.75	(9) Climate	36.25	(5) Physical environment	119.25
(9) Climate	74.25	(c) Too much sleep	21.75	(9) Climate	110.50
(5) Physical environment	66.50	(d) Unsuccessful effort	15.50	(d) Unsuccessful effort	100.00
(c) Too much sleep	28.00	(2) Mental activity	2.75	(c) Too much sleep	49.75

often questionable how far the fault lay with the employer on account of lack of attention to temperature in the plant, and how far with the weather man or the worker himself.

According to such an analysis of the causes of fatigue it would seem that the employer could reach directly little more than half of them and would have to reduce the others by indirect rather than direct methods. The outside activities, including the amount of sleep, are the most important single source of the fatigue feeling, no matter how we look at it.

The second most important cause (see Table 2) seems to be physical activity, though as a single cause it is displaced by wear and tear, or bodily tension. The emotional causes run a consistent third throughout, even if physical activity does tie them for third place in the single cause group. Fourth place would seem logically to belong to the factor of bodily tension, or general wear and tear, since that factor is consistently high; and mental effort as a single cause drops to the bottom of the list.

On looking at the figures pertaining to the individual workers (Table 1), we find these same five causes holding important positions, though the order of their importance varies with the relation of the worker to his total situation. Certain other causes may rank quite high for particular workers whose situation may be somewhat different from the average. For instance, Worker L, next to the youngest of the men and very much interested in his art work, is tired 12.25 periods through too little activity or boredom alone. This figure in his case puts boredom practically on a tie with physical activity for second place by the unweighted method and clearly second by the weighted method. Worker L's heart would often seem to have been elsewhere than in his plant work. Worker H also shows a relatively high percentage of fatigue due to boredom.

Worker S, however, does not show so much tiredness resulting from boredom as the seemingly monotonous nature of his work would lead one to expect. He was faced during the

TABLE 3.—RELATIVE IMPORTANCE OF PLANT AND NON-PLANT FACTORS IN CAUSATION OF FATIGUE

PLANT FACTORS		NON-PLANT FACTORS	
Outside activities	.....	Outside activities	1,040.75
Physical activity	500.00	Physical activity	17.00
Emotional tension	215.25	Emotional tension	215.25
Bodily tension	227.25	Bodily tension	60.00
Mental activity	237.75	Mental activity	.....
Colds, etc	100.37	Colds, etc	100.37
Physical environment	99.00	Physical environment	20.25
Malnutrition	66.87	Malnutrition	66.87
Boredom	121.75	Climate	110.50
Unsuccessful effort	100.00	Too much sleep	49.75
	1,668.24		1,680.74

entire period of the study by a series of very disturbing crises. The nature of his job, by making little demand on his mental ability, allowed the poignant emotions, induced by the crises confronting him, to run riot. Boredom could not exist in the presence of such emotions.[3]

In the case of Worker 3, colds and other minor ailments assume fourth place by the unweighted method and third place by the weighted method. This is due to the hernia and other minor physical ills developed by this worker during the course of the year.

It is for these individual variations from the usual causes that the foreman and plant doctor must be continually on the lookout, as they are often by far the most important in the analysis of the individual case, and at the same time offer the best opportunity for correction. Even the elimination of fatigue must be, in part at least, a problem of the individual approach. Fundamentally it may be true that the only way to reduce fatigue in the perfectly functioning organism is to lower the amount of energy expenditure or build up the bodily energy either by food, or by some other means, but each individual case offers great differences in the best way of applying the general principle.

Our search for the causes of fatigue in the case of the individual worker clearly demonstrates how difficult it is to determine what are the most responsible in the case of either individuals or groups; yet the laws of efficient management today are demanding with ever-increasing insistence that we make a more conscientious effort to find them than we ever have in the past. The evils that excessive fatigue brings in its wake have been proved by many investigators and it need only be mentioned that this study confirms their findings. However, during the trough of the business cycle one often forgets the necessity for being at one's physical best if one is to meet the worries of that crucial time sanely and bravely.

But why lay the burden of elimination on management's shoulders if tiredness results approximately as much from non-plant factors as from those within the plant? Does that condition not imply that the elimination of fatigue is becoming more and more a problem of how the individual worker regulates his life outside the plant? Let me answer these questions indirectly.

There is no doubt that life becomes much happier and saner as the feeling of fatigue is reduced. But the usual attitude toward its elimination seems to be derived from the irrational aspects of the feeling itself. We like to pretend that we are "go-getters" without need of resting, to sleep only at night, and to work continuously from entering a plant or office till noon and from lunch till quitting time, with never a chance to lie down and take a nap. Even the lowly house cat, with his cat naps, may be laughing derisively at our ideas on fatigue prevention.

Just as fatigue may actually result from long-continued boredom—a mental attitude—so a sensible approach to the elimination of that percentage which is unnecessary and harmful would seem to involve the question of

[3] Hersey, R. B.: A Monotonous Job in an Emotional Crisis. Personnel Jour., 1930, *9*, 290.

mental attitude, as much as it does the use of scientific means of detection and elimination. Though the co-operation of many is required to change the public obsession of the perpetual motion man, management and medicine are the logical fields from which to expect sound guidance and instruction.

examination of relative labor turnover, accident rate, faulty work, general irritability, sickness, absenteeism, and production, though they are also symptoms of other industrial diseases, may be helpful in throwing light on the job that is geared at too fast a pace, or on the department in which the physical environment is detri-

TABLE 4.—MEASURES FOR REDUCTION OF FATIGUE CAUSED BY PLANT FACTORS

CAUSE	REMEDY
Physical activity.	Reduction in activity, elimination of useless movements, introduction of machinery; variations in job, provision for rest on job.
Mental strain.	Rest pauses, better training.
Ordinary wear and tear; bodily tension.	Same as for physical activity and mental strain; relief from tension through movement or relaxation.
Emotional tension.	Alert, sympathetic and wise foremen; removal of all unnecessary friction.
Physical environment.	Elimination of detrimental conditions in plant; training in home hygiene.
Malnutrition and improper elimination.	Provision of proper lunch hour and facilities for wholesome food; training in body hygiene and need for exercise.
Colds, etc.	Prompt and efficient medical attention, elimination of plant conditions causing colds, etc.; training in proper care.
Climate.	Regulation of temperature, humidity, and air circulation.
Boredom.	Education in worth of job, provision for variety in activity, rest pauses.

General principles: 1. Expenditure of less energy.
2. Opportunity to recoup before supply of energy is too depleted.
3. Provision of plant environment and atmosphere that is stimulating to the creation of energy.

In the reduction of the fatigue caused by plant factors, the physician and employer have available much helpful information, collected with scientific exactitude by many investigators. Though it is true that exact methods of determining when over-fatigue has set in are not available, an

mental. If the cause can be ascertained, there are certain general measures which can be applied. Some of those which have proved beneficial are given in Table 4.

The channel of approach to a reduction of the outside factors and the obsession of perpetual activity is,

however, still unplumbed. Indirect methods must without doubt be used. Education in sane, individual living is a necessity. Moreover, it is the education of the woman which will count the most; for she, whether wife or sweetheart, is the most powerful stimulus of the outside factors.

Often the same remark was heard, "It ain't money the old woman and I fight about most; it's whether we go out at night." One company, the Philadelphia Rapid Transit Company, has attempted a definite program of education for company wives. At the annual picnic and other collective gatherings of the employees and their families an address is always made to the wives, showing them their rôle as controllers of the family finances, as definite causes of accidents through their nagging and their unwise demands on their husbands; in short, how they function as indirect but important factors in their husbands' plant life. Each time a different phase of the wives' influence is presented as vividly as possible. No direct check on the efficacy of such a plan has proved possible but the company feels that it has been very beneficial, while the wives look forward to this address at each general gathering.

In my contacts with the wives of the workers I was studying, I found them much more receptive to ideas coming from management than their husbands, especially if the ideas came from the president of the firm or some one high in authority. Thus it is that, along with other advantages, reduction in the most powerful single cause of fatigue, the outside activities and personal habits of the individual worker, may be brought about through the education of both workers and their families, provided the employer finds the game worth the candle.

Summary and Conclusions

1. Modern production methods make management responsible for the proper adjustment of the mental and physical requirements of the job to the capacity of the worker. Many worth-while technics have been worked out in the effort to solve this problem, but a final solution awaits the discovery of scientific methods of detecting a harmful amount of fatigue; methods simple enough, however, to apply readily in the shop. In the meantime the subjective side of fatigue in industry, in spite of its importance, has been largely neglected.

2. Workers may feel tired any time. Usually the feeling of tiredness coincides with true fatigue, though this is not always the case. The capacity of the human body to make available varying amounts of energy to meet unusual demands is responsible for this discrepancy. If the energy readily available at the moment is not sufficient to meet the demand of the moment and if the reserves are hard to tap, a feeling of tiredness results. Boredom and the feeling of tiredness may therefore both be the result of a mental or emotional attitude.

3. Though the feeling of tiredness may sometimes be misleading, the study of workers under normal and abnormal "load" indicated that to feel tired more than one-fifth of the waking time as a long-run average is suggestive of an unwise environmental strain or of organic malfunctioning.

Tiredness should also occur irregularly both during the day and over longer periods.

4. Of the various causes of fatigue, the outside activities including efforts at recreation, family duties, and sleep habits are the most important. All told, the employer would seem to be able to reach only half of the causes of fatigue by direct methods. We can, however, still look to the employer—and the physician—for the lead in attempts to reduce the effect of the non-plant causes. The employer gains from better production and a more co-operative and rational working force, as undue fatigue is reduced, no matter what its causes. The professional obligation of the physician is to endeavor to eliminate causes of ill health, among which overstrain is included. The popular obsession of the perpetual motion man can only be erased by wise education in sane living, education directed largely at the woman; for she, whether wife or sweetheart, is the most powerful stimulus of the outside factors.

THE CARCINOGENIC POTENCY OF MINERAL OILS*

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THIS paper is intended to discuss some further experiments on the carcinogenicity of mineral oils with special reference to lubricating oils, each oil being applied to the backs of 100 mice for a considerable period of time. The cancer producing ability of our agents is gauged by the reaction of the mice to the agents. The carcinogenic potency of each agent is given in figures to insure an easy correlation of one result with another.

Some workers give their experimental results in terms of the number of benign and malignant tumors obtained over a given period of time. We have not adopted this procedure because it is not convenient for correlation purposes and because we are of the opinion that a better idea of the relative activity of agents can be gained by utilizing the experimental data available in another manner; and in any case the classification of tumors into only two groups seems to us very inadequate. Nevertheless we consider that the total number of tumors obtained, taken in conjunction with the death rate, is of great importance with regard to the reliability of our potency figures, to be discussed shortly, and in some of our tables we give the tumor numbers in addition to the potency figures. We divide our experiments into first, second, and third class, according to our estimation of the reliability of the figures given. With a certain category of agent, a first class experiment should give at least thirty tumors in thirty weeks, a tumor being added for every week less than thirty and deducted for every week over thirty. Thus a first class experiment of twenty-five weeks' duration should provide us with data relating to thirty-five tumors, and an experiment of fifty weeks with data relating to approximately ten tumors. It must be understood that the number of tumors is of importance only when the death rate of the animals is high; an experiment which gives only one or no tumors in fifty weeks is usually considered to be first class if the animals live well.

Calculation of Carcinogenic Potency

As it is of prime importance that the reader should have an idea of what our figures mean and of the procedure we have adopted in order to arrive at them, we shall first give a few notes with reference to our present method of calculating potency. Our original method (method 1) has been described fully elsewhere (1). The carcinogenic activity is a measure of the response of mice to an agent, but does

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not denote necessarily the concentration of active substances in the agent. Potency is a function of time, so that the higher the potency value, the earlier will the average animal respond. Potency will vary (2) according to:

1. The concentration of units of carcinogenicity in the agent.
2. The amount of the agent applied.
3. The nature of the diluent, if one is used.
4. Possibly, the area covered by the applications.
5. The total number of applications.
6. The frequency of the applications.
7. The susceptibility of the animal.
8. The health of the animal.
9. The greasiness of the skin.
10. The hygienic and dietetic conditions under which the animals are kept—temperature, light, etc.
11. Possibly, the season of the year covered by the tumor bearing period.

In method 1, potency is calculated from graphs of the percentage of living animals whichare bearing or have borne tumors during each week of the experiment, benign and malignant tumors being considered separately. A graph compiled from the average results given by coal gas tars and similarly active substances, when applied to mice twice a week, served as our hypothetical standard to which the arbitrary potency figure of 100 was given. The potency of an agent is computed from the sum of the percentages of living animals bearing tumors during each week of the experiment compared with that given by the hypothetical standard up to a similar period of time. If the abscissas of the graphs are given in weeks from one onward, reading from left to right an agent with a potency above 100 will give a graph situated to the left of the hypothetical standard, while one having a potency below 100 will be situated to the right. The more the graphs diverge from that of the hypothetical standard, the further are the potency figures removed from 100. For example, if upon examination of the results of two experiments of thirty-five weeks' duration, it is found that the sum of the percentages of living tumor bearing animals each week is in one case one-half and in the other case twice that given by the hypothetical standard at the thirty-fifth week, the potency of the two agents under consideration is said to be 50 and 200, respectively.

This method had obviously several defects for which unfortunately at the time of publication of our original paper we were unable to make allowance. We endeavored as soon as possible to eliminate some of these defects, the most important of which are:

1. The length of time a tumor bearing animal remains alive affects the potency figure. In the case of an animal bearing a benign tumor a fallacy is here introduced, which may be serious if malignancy supervenes. In the former case one can safely assume that the tumor does not materially affect the general health of the animal, while a rapidly growing epithelioma induced by a potent agent may be instrumental in causing an early decease of the animal. Consequently there is a fall in the percentage of tumor bearing animals alive and as a rule a still greater fall in the percentage of the epithelioma bearing animals, with a corresponding decrease in potency.

2. We have learned from careful

observation that very early tumors are often not of great significance, so that the potency figure may be rendered too high. Such tumors often disappear, and they, as well as any others which do not persist up to death, would be better discarded altogether, or discounted from the tumor bearing animals during the period when the animal is free from a tumor. Likewise, very resistant animals would be better excluded from our calculations, a single refractory animal in some cases substantially reducing the potency figure.

3. An allowance of ten weeks for a wart or papilloma to become malignant is approximately correct with some agents, but not so with others. We adopted this procedure only for the sake of simplicity, with the full knowledge that it could be improved upon. In the case of potent agents this period is too long, and the potency figure is thereby raised too much; when a weak agent is being considered the potency figure is, for the opposite reason, too low. It may be mentioned, however, that we have met with agents which may be very late in inducing tumors, but once tumors arrive, malignancy rapidly supervenes. We have not meanwhile made any adjustments for this contingency.

4. The graph of the hypothetical standard has the disadvantage that for calculating the potency of an agent which is stronger or weaker than 100, the experimental time period being usually shorter or longer than forty-five weeks, only part of the graph can be utilized, and in some cases only a very small part. Several graphs should really have been made in order to cover the whole field of each experiment one wished to compare.

Recently we have adopted a second procedure to overcome some of these difficulties (see p. 207). In method 2, as soon as any animal had borne a tumor, and the percentage equivalent had been reckoned, this particular animal ceased to exist as far as benign tumor potency was concerned; and once the tumor had become malignant and the percentage equivalent reckoned (malignant tumor potency), the animal took no further part in the potency calculations. As subsequent tumors arose, the figures to be utilized were those obtained by calculating the percentage of fresh animals which bore tumors among the living animals of the experiment, which up to that particular week had shown no evidence of tumor development. The sum of the figures obtained in this way divided by the sum given by the hypothetical standard and multiplied by 100 gives us the benign and the malignant tumor potency, half the sum of the two giving the potency. The figures for the hypothetical standard utilized in method 2 were computed from the average of a large number of experiments.

A consideration of about 5,000 experimental tumors and the change to malignancy has led us to estimate that on an average the latent period for the development of benign and malignant tumors is in the proportion of 2 to 3; *i.e.*, it requires about twice the time for a tumor to develop as it does for the benign tumor to become malignant. Thus in calculating the malignant tumor potency from the hypothetical standard, one-third of the

SPECIMEN OF PROCEDURE ADOPTED FOR CALCULATING POTENCY (P) BY METHOD 2, AND ADDITION FIGURES FOR CUMULATIVE FREQUENCIES

Experiment C.S. 10: Oil 47 daily.

WEEKS	TUMORS	DEAD	LIVING[1]	% × 100	ADD	TOTAL	CUMULATIVE
			Benign				
9	2	..	74	270	1	3	3
10	4	..	72	555	1	5	8
11	4	..	68	588	1	5	13
12	3	..	63	477	1	4	17
13	3	..	59	508	1	4	21
14	2	..	53	377	1	3	24
15	2	..	49	408	1	3	27
16	4	..	47	851	2	6	33
17	6	..	42	1,429	4	10	43
18	5	1	34	1,471	4	9	52
19	..	2	28	.....	..	..	52
20	2	..	26	769	2	4	56
21	1	..	22	455	1	2	58
22	..	1	20	.....	..	..	58
23	1	2	20	500	1	2	60
24	7	..	19	3,684	8	15	75
25	..	2	11	.....	..	..	75
26	..	6	8	.....	..	..	75
27	..	2	7	.....	..	..	75
28	..	2	6	.....	..	..	75
29	2	1	5	4,000	8	10	85
				16,342			
30	..	2	3		..	..	85
31	..	3	3		..	..	85
32	1	1	3		4	5	90
33	..	4	2		..	..	90
34	..	4	2		..	..	90
35	..	1	2		..	..	90
36	..	4	2		..	..	90
37	2	3	2		8	10	100
38	..	2	0		..	..	..
39	..	..	..		..	..	..
40	..	1	..		..	..	..
			Malignant				
28	2	..	34	588	4	6	6
29	1	..	30	333	2	3	9
30	1	..	28	357	2	3	12
31	..	2	26	.....	..	..	12
32	2	..	24	833	5	7	19

[1] Living = Surviving animals which had not previously borne benign and malignant tumors, respectively.

SPECIMEN OF PROCEDURE—*Concluded*

WEEKS	TUMORS	DEAD	LIVING[1]	% × 100	ADD	TOTAL	CUMULATIVE
			Malignant—Concluded				
33	..	2	21	.....	..	..	19
34	..	1	18	.....	..	..	19
35	1	..	17	588	4	5	24
36	2	1	12	1,666	10	12	36
37	1	2	9	1,111	6	7	43
38	..	..	6	.....	..	..	43
39	..	..	6	.....	..	..	43
40	1	..	5	2,000	10	11	54
				7,476			

Hypothetical Standard Divisor

at 29th week = 98
at $26\frac{2}{3}$ " = 74

$\left(40 - \frac{40}{3} = 26\frac{2}{3}\right)$

$\frac{16,342}{98} = 167$

$\frac{7,476}{74} = 101$

$\left.\begin{matrix}167\\101\end{matrix}\right\} \div 2$

134 = P by method 2
104 = P by method 1
238 ÷ 2
P = 119

time is deducted from the date of arrival of the epithelioma, so that if the total malignant figures extend up to forty-five weeks they are divided only by the benign potency figures given by the hypothetical standard at thirty weeks. With regard to the ratio 2 to 3, this only expresses the average malignancy lag. The ratio for synthetic tars approximates more nearly 2 to 2.8, and the ratio for oils more nearly 2 to 3.8. Again, as to the epithelioma lag in the individual animals of an experiment, it is, on the whole, found that the later the development of the so-called benign tumor, the shorter is the epithelioma lag period. Thus the benign-malignant ratio in the animals showing early benign tumors may be 2 to 4.5, and in those showing later tumors it may be more nearly 2 to 2.5. This is equivalent to saying that the epithelium of animals showing no tumor formation may be as far advanced toward epitheliomatous disease as the epithelium of animals bearing a benign tumor. We have not been able to satisfy ourselves that the age of the animal bears any relation to the malignant lag.

In order partially to eliminate very resistant animals, the experiment is only utilized up to the time when there are at least five animals which have not shown tumors. The week during which one or more of these five animals develops a tumor is the last week into which the experiment enters for the calculation of the potency. It would really have been better to have dealt with the animals until less than a certain percentage of the survivors were without tumors. In revising the potency figures we shall probably adopt this procedure.

Our second method of calculating potency introduces again several errors, but on the whole they are not so important as those of method 1. In method 2, early tumors have too low a value, and, conversely, late tumors too high a value. Also tolerance and a certain loss in discarding the last four or so resistant animals are undesirable features. It is obvious that method 2 in some respects gives errors in the opposite direction to method 1, and a study of the potency figures obtained by both methods from the results of some 400 experiments has led us to take an average of the two methods as our final potency of any particular agent. Thus all figures given in this paper refer to the average figures given by the two methods we adopt for making our calculations; as more experimental data become available we shall doubtless again alter our procedure, and probably exclude method 1 altogether.

Method 2 is valuable in that it gives us directly the percentage of living animals which develop tumors after different periods of exposure to our agents. We are of the opinion, however, that a better procedure would be to calculate the potency on the basis of mouse susceptibility alone (see p. 207). The mouse susceptibility would be given directly by the sum of the number of fresh tumors which arose during each week of the experiment among the living animals plus the equivalent number which it is presumed would have been given by the non-tumor bearing animals, had they lived. In this case, mouse susceptibility could be given as 100 or less, from which figures the potency could be deduced in a manner most convenient for the recording of the activity of our agents. Examples of mouse susceptibility to mineral oils are given in Table 5.

We should like to draw attention to one further point with regard to the estimation of carcinogenicity of agents, which appears to us to be of great importance for obtaining as true a criterion as possible of their relative activity. In general terms it can be said that investigators working on the cancer producing ability of different substances habitually record their results in terms of benign and malignant tumors developed among their animals. In our opinion the value of all such investigations, including our own, would have been enhanced had the grouping of the tumors been more elaborate. We consider that the tumors should be classified into at least six groups instead of two, for the whole process from the hyperplasia of the epithelium to the development of a rapidly growing epithelioma, metastasizing in distant organs, is that of a gradual sequence of changes so insignificant and obscure as to baffle any means we have, or are likely to have, to demonstrate them to our senses. It is a summation of these changes only which under certain circumstances permits us to diagnose one tumor as benign and another as malignant. A measure of our impotence is the frequent occurrence of tumors of doubtful nature which cannot with confidence be placed in either of the foregoing two categories. They may have a tendency in the one or other direction, and may be classified accordingly, but these subdivisions will later again need to be subdivided and so on, until finally further sub-

division is beyond our capabilities. But because it is illogical biologically to divide tumors into benign and malignant, we feel that our potency figures would be considerably improved if we, so to speak, decreased our class interval, and instituted six classes instead of two. This question will occupy our serious attention when facilities allow the extra work involved to be carried out.

Although our potency figures indicate the extent of the response of the mouse to an agent, they do not tell us the concentration of carcinogenic material in the agent. As stated in previous publications (1) (2), a unit of carcinogenicity will if possible be established by physical and chemical means, so that ultimately the carcinogenicity of agents can be found without the routine use of animals. Some of the physical characteristics are given in the tables relating to the potency of the oils, but we are anticipating more useful information from an estimation of the reduction of permanganate by the oils, their iodine values, etc. Unfortunately these last-mentioned investigations which were being undertaken by our collaborator, Dr. Fulton, have had to rest in abeyance for a while, but from his provisional estimations it appears that data of real value for the establishing of the unit of carcinogenicity might be obtained from these or similar methods.

Our original standard experiment in which the applications of the agents under test were made twice a week has now been practically abandoned in favor of the more frequent applications of five times a week (daily experiment). As we have pointed out elsewhere (2). when dealing with weak agents especially, much more reliable results seem to be obtainable when the method of frequent applications is utilized; this conclusion is based on many experiments with agents applied by both methods. In order to correlate our former results with those we are getting at the present time it has been found useful to calculate what the approximate results would have been by the method of daily application. When more of the double experiments have been performed it should be

TABLE 1.—RELATION OF APPLICATION FREQUENCY TO POTENCY[1]

POTENCY		CONVERSION FACTOR
2 Applications per Week	5 Applications per Week	
0.1–0.9	3.3–22.5	33–25
1	23	23
2	42	21
3	57	19
4	68	17
5	75	15
6	84	14
7	91	13
8	96	12
9	99	11
10	100	10
15	135	9
20	160	8
25	175	7
30	180	6
35	192	5.5
40	200	5
50	225	4.5
60	240	4
70	245	3.5
80	260	3.25
90	270	3
100	280	2.8

[1] Where actual experiments have not provided us with the necessary figures, we have filled in with the approximate figures which theory demands.

possible to institute a formula for the conversion of one kind of experimental result to the other, although the matter is not quite simple because of the great difference in the influence of frequency of application on the tumor yield by very weak and very strong agents. Meanwhile, for the conversion of standard to daily experiments we utilize Table 1, in which will be seen the extent of the fall in the conversion factor as the activity of the agent increases. On the whole, experiments with moderately strong agents are more reliable than those with very weak or very strong agents, so that for comparative experiments, when possible, we aim at getting a good yield of tumors with a resulting potency figure of about 500. In order to obtain well-marked differences when testing the effect of any variable factor, it may be better to use weak agents or if strong agents are used, to paint the animals infrequently; but the results obtained when utilizing weak agents, although they may show wide differences, are usually not very reliable. Variability of susceptibility of the animal plays too important a part when dealing with weak agents; consequently they are the best type of agent to show up animal variability. On the other hand, if in conducting the experiments care is taken to arrange matters so that as far as possible the ultimate potency figures of the control lie somewhere between 50 and 1,000, the effect of the factor under test may not be so obvious as it would have been had the potency figures been well below this range, but the reliability of the results should be very much greater.

Thus, in drawing conclusions from our results, there are two important considerations to be kept in mind: (1) the animal death rate and (2) the animal susceptibility variant. As we have remarked previously, if the death rate is too high the potency figures obtained are relatively of little value, and so also are those obtained if the average susceptibility of the batch of animals used is not within normal limits. We shall see that several of our experiments gave very irregular results, and it seems that in many cases the irregularities were unavoidable. No method of estimating potency could seemingly place two experiments in line if the two batches of animals used had not approximately a similar average mouse susceptibility. In some cases repetition of an experiment has been deemed necessary, but in other cases we are able to surmise the degree of irregularity from a series of closely related experiments. This is, of course, where a great advantage is gained by the utilization of a large number of animals, the frequency and extent of the irregularities indicating to us the relative value of our results as a whole. We have not hesitated to dwell upon this question for we feel that it is of more than ordinary significance both to ourselves and to others who are engaged in similar lines of investigation. This leads us to another aspect of the subject which requires consideration.

Before we enter into the question of the carcinogenicity of mineral oils, we feel that a word of caution is due to those who are not familiar with the production of the oils and their commercial distribution; to those who have, so to speak, spent their lives among oils, the remarks we are about

to make may perhaps appear unnecessary. We have divided the oils tested into groups, according to their presumed field of origin. We say "presumed," because although an oil may be supplied to us as originating from a certain field or country, it is not necessarily to be assumed that the oil in question was correctly designated. *Also it is extremely important to bear in mind that the oils tested by us are only isolated samples: the productive fields of a country may be numerous, each field yielding a different type of oil or even the same field yielding several types, according to the depth of the drilling, etc.; therefore caution must be exercised in drawing conclusions from our results. Similarly, with regard to shale oils, we know that the oil shales vary considerably as to their quantitative yield of oil, and we have no proof that they do not vary carcinogenically. Therefore it is not to be presumed that all shale oils would give potency figures similar to those obtained by us with such oils.*

Having completed the preliminary remarks on the calculation of potency, needed for an intelligent interpretation of our results, we shall now proceed to examine our investigations with the Scotch shale oils tested, and subsequently deal with ordinary petroleum and other oils.

Carcinogenic Activity of Crude and Refined Shale Oils

The carcinogenic potency of shale oils was found by Leitch (3) to be very much greater than that of the petroleum well oils, and we ourselves obtained similar results from our experiments along these lines (4). Further animal tests of different samples of shale oil have more recently been made in these laboratories. Leitch had already examined most of the shale products, but we were interested in aspects of the subject other than those directly concerning tumor formation.

The results of our experiments so far completed are given in Table 2. Oil 25 is the crude oil obtained from oil shale retorted at about 700°C. (internal temperature), the scrubber naphtha and ammonia liquor distilled from the shale being removed. From oil 25, crude naphtha, burning oil, resin, and coke, are removed by distillation, and the heavy oil 41, which contains the whole of the solid paraffin wax, is obtained. Some of the wax being removed by presses, oil 40 (blue oil) is obtained, which yields on distillation various oils, all of which contain a certain proportion of the paraffin wax. Of these various oils we have investigated only the lubricating oil from which the bulk of the residual wax has been pressed, oil 37. This unfinished lubricating oil is treated commercially with about 4 to 5 per cent. of pure sulphuric acid, usually added in two portions, and after removal of the tar, the oil is washed with soda ash solution, the latter being drawn off after steaming at about 52°C. The oil is then washed with water and subsequently allowed to settle in tanks, when it is marketed as the finished lubricating oil, oil 39.

The oils enumerated were tested by the procedure adopted in what we call our daily experiment, and on referring to Table 2 it will be seen that the highest potency figure was given by the unfinished lubricating oil from which practically all the paraffin wax had

been removed, but which had not been refined by treatment with sulphuric acid and filtration. The relative potencies are calculated from this oil, the percentage decrease in potency of the other oils being then at once apparent. Some of the cruder oils were less than one-third as active as the unfinished lubricating oil; the difference was due apparently to the presence in the former of inactive products which are removed later.

In the samples tested by us, it will be noted that the commercial treatment of the unfinished oil (oil 37) with 4 to 5 per cent. acid reduced the potency approximately 33 per cent. (oil 39). This seems to us a rather poor result, for the oils treated with a similar amount of acid in these laboratories have usually a greater percentage reduction in activity. The difference, we imagine, is due to the fact that our oils have already been treated commercially with acid, and thus, being clean oils, no part of the acid we utilize is wasted by reacting upon some of the non-carcinogenic contaminating material. In order to investigate this question we are testing the relative effect of a given quantity of acid on an oil before and after filtration. We anticipate that when the acid treatment follows filtration, we shall obtain a less potent product than when the processes are reversed, although to obtain a bright appearance of the final

TABLE 2.—CARCINOGENIC POTENCY OF CRUDE AND REFINED SHALE OILS

OIL NO.	PRODUCT	POTENCY	RELATIVE POTENCY[1]
25	Crude oil; coke, scrubber naphtha, ammonia removed	118	35
41	Heavy oil; containing the whole of the wax	97	29
40	Blue oil; part of wax removed	90	27
37	Unfinished lubricating oil; almost all wax removed	338	100
39	Finished lubricating oil	228	68
28	Similar to no. 39 (sample 2)	216	64
55	Similar to no. 39 (sample 3)	244	72
27	Of a little lower viscosity than no. 39	179	53
8	Of a little higher viscosity than no. 39	258	76
	Second test of same sample	293	87
44	Crude oil; experimental retort at 500°–800°C.	88	26
43	Crude oil; experimental retort below 500°C.	132	39
54	Crude oil; experimental retort below 400°C.	60	18

[1] Compared with the unfinished lubricating oil as 100.

We hope later to be in a position to test all the other shale products, although Leitch has already shown that there is a difference in activity of many of them, the lower boiling spirits being nontoxic, while the burning oils are toxic. It is important to remember that the percentage of lubricating oil from the crude oil ranges about 6 per cent., so that a good proportion of carcinogenic material in the crude would appear to find its way into the other products.

product filtration should follow the acid treatment. Our experiments on the acid treatment of oils, together with other methods of detoxication, will be discussed in a subsequent paper.

Our next investigations consisted in an examination of shale oils retorted at different temperatures. Messrs. Scottish Oils, Ltd., kindly undertook to prepare the oils for us in their experimental retorts, the following three oils being provided from their laboratories: oil 44 retorted at 500° to 800°C.; oil 43 retorted below 500°C.; and oil 54 retorted below 400°C. While the oil manufactured at a temperature not exceeding 400°C. had a low degree of activity, we were surprised to find that the other two oils were both fairly active, oil 43 for some reason giving a higher figure than oil 44. From previous experiments on the manufacture of synthetic tars at different temperatures (5) we rather expected that as oils 43 and 54 were crudes, they would at the most not have a potency greater than refined petroleum well oils. Our experiments lead us to believe that oil shale contains compounds easily rendered carcinogenic on being retorted at a relatively low temperature, while at a higher temperature additional and more active compounds are formed. We are at present testing the effect of relatively low temperatures on the potency of carcinogenic and non-carcinogenic oils, in order to ascertain the degree to which active compounds can be manufactured from different substances subjected to various temperatures. The most we can say at the moment is that medicinal liquid paraffin, autoclaved at a temperature of 380°C. at a pressure of approximately 50 atmospheres, is showing definite evidence of activity, several tumors having already been registered among the animals painted for less than four months. One wonders what potentialities there are when such an oil finds itself in the presence of a catalyst in the alimentary canal, and we are proceeding as a preliminary to prepare oils heated in the presence of a catalyst, for test on animals.

Carcinogenic Potency of Straight Petroleum Oils

For those who are not familiar with the composition of petroleum oils it may be stated that the constituent hydrocarbons are usually roughly divided into four groups: naphthenes, paraffins, aromatics, and asphalts. All oils have examples of the four groups in their constitutions; but the percentage amounts of each may vary, and particular oils may be classified accordingly. Thus certain Russian oils are sometimes spoken of as naphthenic, some Pennsylvanian as paraffinic, and some Borneo as of aromatic base; or an oil may be spoken of as of mixed base.

In Table 3 will be found a list of the oils tested by us, with their presumed origin and some of their physical characteristics. The latter were supplied, together with the oil samples, by courtesy of the oil companies mentioned later. From this table it will be seen that there is a great difference in the results obtained with the various oils, some apparently having a high degree of activity as compared with others. We would draw special attention to the fact that several of the experiments are designated as class 2;

TABLE 3.—CARCINOGENIC POTENCY OF SAMPLES OF MINERAL OILS WITH STATED ORIGIN

STATED ORIGIN	OUR NO.	SPECIFIC GRAVITY	FLASH POINT		VISCOSITY, REDWOOD		DURATION OF EXPERIMENT	CLASS OF EXPERIMENT[1]	TOTAL TUMORS		POTENCY
			Open	Closed	70°F.	140°F.			Benign	Malignant	
							wks.				
Venezuelan	47	0.923	...	325	279	57	40	1	40	11	119
	47U[2]	0.928	...	325	251	57	40	1	29	6	177
	47U[2]	(special diet)			...	...	35	1	56	6	276
Borneo	69	0.938	...	345	319	...	25	2	18	1	175
	49	0.948	320	290	189	49	40	1	24	3	64
	45	1.000	370	345	...	359	40	1	21	0	30
Persian	61	0.906	...	370	270	...	30	2	20	1	175
	23	0.910	...	393	400	...	40	2	4	1	43
Californian	50	0.923	325	310	196	50	40	1	31	2	86
	73	0.932	370	360	1,366	118	20	2	4	0	10
	9	0.937	...	364	1,300	...	30	1	12	1	50
Mid-continent	6	0.873	...	297	98	...	..	2	5	0	57
	51	0.915	340	315	202	52	40	1	17	2	50
Roumanian	68	0.926	...	315	180	...	25	2	16	0	45
Mexican	66	0.902	...	345	163	49	25	1	16	0	41
	66U[2]	0.905	...	345	163	49	25	1	22	1	57
	31	0.905	...	330	165	50	50	1	22	2	36
	32	0.915?	...	385	370	70	50	1	2	0	3
Venezuelan and Mexican blend	34	0.920	...	350	300	60	40	1	18	1	37
	35	0.923	...	350	400	69	40	1	25	1	44
	36	0.928	...	350	500	75	40	1	13	1	34
Texas	33	0.917	...	375	390	...	40	1	15	2	30
	71	0.918	330	310	218	52	20	2	1	0	2
	72	0.921	360	340	469	69	20	2	3	0	5
	10	0.929	...	367	1,550	...	50	1	0	1	1
Pennsylvanian	70	0.874	405	380	295	64	20	2	1	0	2
	29	0.890	...	360	290	62	50	1	8	0	3
	11	0.890	...	380	320	...	45	1	4	0	2
	59	0.895	...	370	290	...	30	2	20	0	17
	30	0.895	...	380	380	...	50	1	14	0	10
	7	0.895	...	383	400	...	45	1	10	0	8
Russian (Balachani)	58	0.897	...	370	390	68	30	1	3	0	3
	63	0.900	...	370	390	...	30	2	8	0	9
	57	0.909	...	400	1,200	134	30	1	1	0	1
	56	0.913	...	420	2,720	210	30	1	0	0	0
? Pennsylvanian blends	3	0.884	...	392	400	...	25	2	1	2	66
	19	0.895	...	343	200	...	35	2	4	1	45
Slab oil ? Russian	4	0.857	...	348	150	...	25	2	0	0	0
Medicinal liquid paraffin ? Russian	22	.....	...	...	...	...	60	1	0	0	0
Medium motor ? Origin	53	.....	...	...	...	...	40	1	4	0	4
	53	Removed from engine sump					40	1	9	1	12
Diesel fuel oil ? Origin	24	.....	...	...	...	...	45	1	15	3	28

[1] *I.e.*, value of results.

[2] Unfinished lubricating oil.

i.e., the margin of error is possibly large. Oils 61 and 69 are presumably active oils, but the potency figure of 175 is probably too high, while with oil 23 the figure may be too low. When estimating the value of the figures obtained from each experiment we analyze all aspects of the experimental conditions and draw our conclusions accordingly. For example, on referring to the list of oils given, it will be noted that in a few cases we have queried the field of origin. This has been done where the origin is more than usually doubtful. Two important doubtful oils are nos. 19 and 3, which were oils marketed as of Pennsylvanian origin, and supplied to us direct by cotton spinners. These oils are viewed with suspicion both on account of the irregularity of the potency figures obtained and because of the fact that they both yielded very potent high boiling fractions on distillation (4). As we shall see later, the fact that no. 19 was said to be a blend of Pennsylvanian with 20 per cent. sperm oil renders our results still more remarkable. If we compare the potency figures given in the table for the Pennsylvanian oils with those given by oils 19 and 3, we appreciate that something appears to be wrong, and on finding that the high boiling distillates obtained from oils nos. 7 and 11 yielded products less potent than in the case of oil 3, our doubts were increased.

The discrepancy in the potency figures obtained from our examination of the Mexican oil no. 32 compared with the other two oils of the group also needs explanation. For biologists who have not studied oils, animal variations may appear sufficient to account for the discrepancy, and for those commercially interested in oils, normal variations in samples of Mexican origin may appear sufficient. Furthermore, statisticians may be satisfied that our methods of arriving at our potency figures leave room for such a discrepancy to arise. We, ourselves, are not willing to admit that any of these explanations is adequate, but are more inclined to cast doubt upon the designation of the oils in question. Of course it may have originated from Mexico, but from a relatively harmless crude of a different field to the other two oils, or it may have had an unusually intensive acid treatment. On the other hand, the iodine value we obtained suggested that our potency figures should have been higher. Unfortunately, we had no surplus oil with which to test for sperm or other saponifiable oil, the presence of a small quantity of which would be sufficient to account for our low potency figure and the relatively high iodine value. The specific gravity and viscosity would, of course, then have to be taken into consideration.

From earlier experiments on the oxidation and reduction of oils, we had formed the opinion that the aromatic hydrocarbons were chiefly instrumental in inducing carcinoma in animals (6), and our experiments with straight oils have served to strengthen this view. It is sometimes said that crude oils, before distillation, contain very little or no aromatic compounds, the latter being synthetized during distillation. This may or may not be the case, but it cannot be denied that

in some substances, at least, crude oils are capable of inducing tumor development in animals.

The oils of each field can be conveniently divided into two groups: spindle oils and the heavier grade oils, such as engine oils. On the whole, there is a tendency for the heavier grade oils to be less active than oils used in the textile industry. This may be partly due to the average lower viscosity of the spindle oils, although with shale oil we found that lowering of the viscosity lowered the potency figures obtained. The fact that the heavier oils are as a rule refined with a higher percentage of acid than the lighter spindle oils which are more easily refined, is probably in a large measure responsible for the difference in our results with samples of varying gravity from the same field. It is well to remember in considering the question of viscosity that even the very viscous crude oils, containing an abundance of paraffin wax, flow freely when in contact with the warmth of the animal's skin.

It will be noted that in some cases we have performed two or more tests on what appear from the physical characteristics to be similar oils. This has been done with the intention of verifying the equality of trade samples obtained through different channels, and at the same time we gained valuable information as to the accuracy of our methods. Also, by massing a group of experiments, errors are less likely to arise, in view of the large number of animals involved. The average activity of the oils from the point of view of field of origin is given in Table 4; the total number of animals utilized in each case is shown. In this table the relative potency of the oils

TABLE 4.—RELATIVE CARCINOGENIC POTENCY OF MINERAL OILS COMPARED WITH SHALE OIL AS 100

STATED ORIGIN	REMARKS	NO. OF ANIMALS USED	RELATIVE POTENCY
Scotch shale	Crudes	300	39
	Unfinished lubricating	100	144
	Finished	600	100
Venezuelan	Unfinished lubricating	200	77
	Finished	100	51
Borneo	Finished	200	41
	Residuum	100	13
Persian	Finished	200	37
Mid-continent	Finished	200	23
Californian	Finished	300	16
Roumanian	Finished	100	15
Mexican	Unfinished lubricating	100	19
	Finished	300	9
Mexican and Venezuelan	Finished	300	16
Texas	Finished	400	3
Pennsylvanian	Finished	600	2.4
Russian	Finished	400	1

compared with shale oils as 100 is given, so that the comparative activity of the oils is seen at a glance.

In Table 5 we have divided forty experiments of 100 animals each into four groups of ten experiments, according to the potency figures which we obtained from oils of different fields. Cumulative figures only are given, but it is an easy matter to obtain from these the individual susceptibility of the members of an average batch of 100 animals to the different oils.

wish to know how long it will be before the Russian-Pennsylvanian oil series will have forty-one individuals showing tumors, we can predict this state of affairs to occur at about the fiftieth week of contact on a presumed death rate of nil. We are able to deduce this approximate date from a study of the average mouse response period, in experiments entailing the utilization of some 50,000 animals with various agents of widely different carcinogenic activity.

TABLE 5.—AVERAGE MOUSE SUSCEPTIBILITY, PER HUNDRED[1]

OIL MARKETED AS	WEEKS								
	5	10	15	20	25	30	35	40	45
Cumulative Benign Tumor Frequency									
Shale	0.3	14.0	41	66	90	..	..	..	..
Venezuelan, Borneo, Persian, Californian	0.3	7.0	25	51	65	70	80	..	..
Mid-continent, Mexican, Texas	0.1	2.0	12	24	34	46	71	..	..
Pennsylvanian, Russian	0.0	0.1	1	6	11	13	20	24	..
Cumulative Malignant Tumor Frequency									
Shale	..	..	0.1	3.0	13	34	65	..	..
Venezuelan, Borneo, Persian, Californian	..	..	0.2	0.6	2	6	16	43	..
Mid-continent, Mexican, Texas	..	..	0.0	0.0	0	0	3	17	..
Pennsylvanian, Russian	..	..	0.0	0.0	0	? 0	? 0	? 0	? 0

[1] 1,000 animals were used in each of the four groups.

It will be of some interest to examine for a moment the two extreme members of the series—the Russian-Pennsylvanian and the shale oils. The figures indicate that if two series of mice each containing a similar number of individuals are placed in contact with our Russian or Pennsylvanian and shale oil for a similar period of time, say fifteen weeks, the proportion of individuals bearing tumors in each series will be about one to forty-one. If we

We have attempted to apply our results with animals to man, in an endeavor to get an idea of the approximate tumor expectancy among workers exposed daily to contact with different lubricating mineral oils. We have adopted the simple procedure of assuming the response of man in years to be equivalent to the response of the mouse in weeks, but we have no proof that this procedure gives a true index of man's relative susceptibility.

J. I. H.
June, 1931

Based on this assumption we can compile a table (Table 6) showing the presumed percentage liability of workers exposed to our oils to develop malignant tumors after from ten to fifty years' contact (compare also Table 5). This table refers to men who are in daily contact with the oils. Occasional absence from contact, especially if for periods of weeks or months, should lengthen the latent period very materially. Table 1 shows clearly the importance of frequency of contact, especially in the case of weak agents. From a consideration of what actually happens among mule spinners, and from the percentage of cases of epithelioma met with among those having been spinners for from ten to fifty years, one might be able to form an approximate idea of the carcinogenicity of the oil to which they have, on the whole, been exposed. We have dwelt on this question because we wish to draw attention to the practical importance of the difference in the activity of the oils as marketed according to the field of origin, and, consequently, the relative number of cases of cancer which might occur from contact with them. According to our way of considering the subject, a man working in contact with our shale oils for twenty years is as likely to develop cancer as one working in contact with our Pennsylvanian oils for fifty years; or at any given period of contact with spindle oils the worker in contact with the shale oil is roughly fifty times more liable to develop cancer than the worker in contact with the Pennsylvanian oil.

TABLE 6.—APPROXIMATE PERCENTAGE LIABILITY OF SURVIVORS TO DEVELOP CANCER AFTER CONTACT WITH LUBRICATING OILS FOR TEN TO FIFTY TIME PERIODS[1]

Shale oil = 100% at 50 time periods.

OIL MARKETED AS	TIME PERIODS				
	10	20	30	40	50
Shale	0.20	2.00	10.0	50.0	100
Venezuelan	0.10	1.00	5.0	25.0	51
Borneo	0.08	0.80	4.0	20.0	41
Persian	0.07	0.70	3.7	18.0	37
Mid-continent	0.05	0.46	2.3	11.0	23
Californian	0.03	0.32	1.6	8.0	16
Roumanian	0.03	0.30	1.5	7.5	15
Mexican	0.02	0.18	0.9	4.5	9
Texas	0.01	0.14	0.7	3.5	7
Pennsylvanian	0.004	0.04	0.2	1.0	2
Russian	0.002	0.02	0.1	0.5	1

[1] This table is based on our potency figures obtained from the results of tests on a selected number of oil samples. If the relative response of man is similar to that of the mouse, and if contact with the oils is continuous, the time period for man, we imagine, should be in the neighborhood of years. If, on the other hand, the malignant tumor lag in man more nearly approximates that in the rabbit, the time period would be considerably extended.

Examination of Blends of Mineral Oils

Among the many agents tested which we have found apparently to possess no carcinogenic activity were included samples of vegetable and animal oils (7). Sperm, olive, rape, cottonseed, and neat's-foot oils failed to induce tumors when applied to mice, even under the most severe experimental conditions. Likewise medicinal liquid paraffin has given consistently negative results; while mineral oils, treated less thoroughly with acid and still retaining some of their yellow coloration, will often give no tumors, the carcinogenic substances which may remain being either too weak or too inadequate in amount to be effective in inducing a demonstrable response in our animals. Meanwhile, however, we consider that all colored mineral oils should be viewed with suspicion until further experiments have given us additional information on the efficacy of acid treatment. For instance, we do not assume that the mineral oils utilized for making up cosmetics and hair oils are non-carcinogenic, although such oils are usually highly refined.

In previous papers (2) (8) we have mentioned that lanolin seems to have a beneficial effect in delaying the advent of tumors among animals painted with a carcinogenic agent; in order more thoroughly to investigate this aspect of the problem we have prepared several blends of mineral oil with animal and vegetable oils. Practically all workers who have investigated the effect of lanolin applications or lanolin feeding on animals painted with gas tars and pitch have come to the conclusion that the development of tumors is hastened among animals subjected to lanolin treatment. These observations are of course diametrically opposed to our own observations with mineral oils and synthetic tar; but there are good reasons why gas tar should act differently to our agents. The harmless oils we have up to the present used for making the blends are: lanolin, sperm, and liquid paraffin. From 1 to 20 per cent. of one or more of these oils was blended with shale oil and Mexican, Pennsylvanian, Persian, and Russian spindle oils, the resulting tests on animals indicating most clearly a striking decrease in the potency of the blends as compared with the straight mineral oil control. The experimental results of this group of experiments are given in Table 7. It may be well to mention in passing that the Mexican blends were not made up with oil from the same sample as that utilized for the control experiment. Contrary to our expectations some experiments with shale oil-paraffin wax blends, now in progress, are indicating rather an increase than a decrease in potency. We are somewhat intrigued with the early indications, but we must leave these incomplete experiments for discussion at a future date.

Beyond the fact of the general decrease of potency by addition of the harmless oils, it is of interest to note that the decrease in potency by no means runs parallel with the amount of saponifiable oils used. For instance, 5 per cent. sperm is not very much less efficacious than 20 per cent. sperm; the same applies to the lanolin blends; and in some cases our figures are reversed. We may remark in passing that when attempts are made to detoxicate oils with sulphuric acid, a subject

which we shall discuss in a subsequent paper, it is found that the decrease in activity of the acid treated oils is not proportional to the quantity of acid used. This seems to be especially noticeable between an acid range of 1 to 10 per cent. A strikingly irregular result was registered with the 20 per cent. sperm-Mexican blend, evidently control to this series of blends, a further series was made with the Texas engine oil 10, an oil which in the pure state had a potency figure of only 1, and was the nearest approach to a negative oil we had tested. Oil 10 was evidently a borderline oil, its carcinogenicity being of such a mild degree that it was able to induce a tumor only

TABLE 7.—BLENDS OF MINERAL OILS WITH SAPONIFIABLE OILS

OIL MARKETED AS		SAPONIFIABLE OIL		DURATION OF EXPERIMENT	TOTAL TUMORS		POTENCY	RELATIVE POTENCY
					Benign	Malignant		
	%		%	*wks.*				
Shale	100	Sperm	0	35	25	2	293	100
	95		5	35	28	10	92	31
	90		10	35	24	2	87	30
	80		20	35	37	9	68	23
Mexican	100	Sperm	0	50	22	2	36	100
	95		5	45	12	0	6	16
	90		10	45	4	0	1.5	4
	80		20	45	19	1	23	64
Pennsylvanian	100	Sperm	0	30	20	0	17	100
	80		20	30	4	0	4	24
Persian	100	Sperm	0	30	20	0	175	100
	80		20	30	18	0	30	17
Russian	100	Sperm	0	30	8	0	9	100
	80		20	30	4	0	3	33
	0		100	70	0	0	0	0
Shale	90	Lanolin	10	35	17	4	31	11
Mexican	99	Lanolin	1	25	15	0	24	66
	95		5	25	15	0	20	55
	90		10	25	4	1	9	11

due to variation in mouse susceptibility.

A further group of experiments of which the results are given in Table 8 were instituted to gain an idea of the actual effect of dilution alone. For this purpose 5, 10, 25, 50, and 75 per cent. shale oil was blended with liquid paraffin, the latter oil being considered to be absolutely inert. By way of in exceptionally susceptible animals. The concentration in carcinogenic units was insufficient to enable the hyperplastic epithelium to enter into the malignant phase. An examination of the figures given in the table shows but little difference in activity of the liquid paraffin and the Texas oil blends, except in the lower three dilutions where the unit of carcinogenicity

in the shale oil was, so to speak, buffered up by the carcinogenic unit in the Texas oil. In the higher two dilutions the Texas oil blends are presumed to have met with more resistant animals than in the case of the liquid paraffin blends. Further, the results of the blend of 75 per cent. shale oil with liquid paraffin are used for comparison with the saponifiable

TABLE 8.—BLENDS OF SHALE OIL WITH OTHER HYDROCARBON OILS

SHALE OIL	OTHER HYDROCARBON OIL		TOTAL TUMORS		POTENCY	RELATIVE POTENCY
			Benign	Malignant		
%		%				
100	No. 22[1]	0	25	2	293	100
75		25	25	2	142	48
50		50	26	15	122	42
25		75	13	2	9	3
10		90	0	0	0	0
5		95	1	0	0.3	0.1
0		100	0	0	0	0
75	No. 10[2]	25	21	3	110	38
50		50	25	2	85	29
25		75	14	2	12	4
10		90	12	0	10	3
5		95	8	0	4	1
0		100	0	1	1	0.3

[1] Medicinal liquid paraffin.
[2] Texas engine oil.

oil blends, and on the assumption that the liquid paraffin is inert one can estimate the efficacy of the protective action of the vegetable and animal oils. Incidentally one is enabled from the results with oil 10 to get a vague notion of what one may call the concealed units of carcinogenicity of an agent, *i.e.*, the maximum number of units of carcinogenicity which cannot be demonstrated by the induction of tumors but is utilized in exciting the preliminary hyperplasia of the surface epithelium.

Relation of Fluorescence to Carcinogenicity

Brooks and Bacon (9) state that the fluorescence of mineral oils is due to substances related to chrysene; and it may be of interest to mention here some experiments we have performed with chrysene. Among many pure hydrocarbons which we have tested, chrysene alone has so far given more or less consistently a certain number of tumors in mice painted with it. Since this compound is very insoluble, we have been obliged to use it as a *Krystallbrei* in such diluents as liquid paraffin or oleic acid. Recently by utilizing the latter diluent and resorting to the intensive method of application, we have succeeded in obtaining a good yield of tumors, so that a chrysene-oleic acid *Krystallbrei* has quite an appreciable potency figure. The solubility of chrysene in oleic acid at 40°C. (about the body temperature of the mouse) is 0.15 per cent., and if, as is probable, it is only the part in solution in the *Krystallbrei* which is effective, chrysene has really a high degree of activity (*cf.* synthetic tar dilutions (2) (5)). While liquid paraffin is a negative agent, oleic acid (Kahlbaum) gave a potency figure of approximately 4. Chrysene in the former diluent gave a figure of 4, while in the latter diluent it mounted to 23. The details of these experiments are given in Table 9.

These experiments have a bearing on our examination of mineral oils because we are of the opinion that the carcino-

genicity of oils is possibly not unrelated to the type and degree of fluorescence present. Given two oils of similar specific gravity and viscosity which have been refined in a similar manner, we anticipate that the greater the degree of fluorescence the more potent will the oil be found to be. Also oils having a blue fluorescence seem on the whole more active as cancer producers than those having a green fluorescence. In our endeavors to separate an oil into an active and an inactive portion it has sometimes been noticed that the inactive, or relatively inactive, portion has lost most of its original fluorescence, the active portion having a higher degree of fluorescence than the original. We have not gone into the question of permanent or transitory loss of fluorescence. Two recent publications by Kennaway and Hieger (10) (11) on carcinogenic substances and their fluorescence spectra will be found of great interest to all workers in the domain of cancer research, and especially to those carrying out investigations similar to our own.

TABLE 9.—CARCINOGENIC POTENCY OF CHRYSENE

AGENT	DURATION OF EXPERIMENT	WEEK OF FIRST TUMOR		TOTAL TUMORS		POTENCY
		Benign	Malignant	Benign	Malignant	
	wks.					
Liquid paraffin	60	..	..	0	0	0
Oleic acid (Kahlbaum)	60	7th	..	5	0	4
7.5 per cent. chrysene in liquid paraffin	78	38th	48th	6	1	4
7.5 per cent. chrysene in oleic acid	50	23rd	40th	18	9	23

Discussion on Relative Carcinogenic Activity of Mineral Oils

If the exigencies of the trade demand the utilization of mineral oils for lubrication purposes to the practical exclusion of saponifiable oils, we have to consider which among the mineral oils are the safest to recommend. From our animal tests it is manifest that the oils which we utilized, marketed as of Russian and Pennsylvanian origin, are substantially less active than the majority of the other oils tested, and if it is assumed that the relative response of man is similar to that of our animals, exposure to our shale oils would be approximately fifty times more dangerous than exposure to the former two types of oil. A consideration of the tables reveals that with the exception of the two doubtful oils nos. 3 and 19, we have not so far succeeded in obtaining a single malignant tumor with a straight Russian or Pennsylvanian oil. Such oils must, however, be viewed with suspicion, first because we are conservative in our diagnosis of malignancy, some of our so-called benign tumors having appearances which in human pathology we should feel bound to consider as malignant; and secondly because methyl sulphite and alcohol extracts of some of these oils have given tumors which were unquestionably malignant.[1] Although the use of

[1] Since this paper was written, malignant tumors have been found among animals

shale oil in the textile industry might be discontinued without much inconvenience, the difficulty becomes more real when some of the other oils are considered ; but we would repeat again here that great caution is necessary in forming a judgment as to what oils are good and what are bad. *Although we ourselves have an immense amount of experimental data available, we do not feel justified at the present juncture in making any dogmatic statements on the relation of the origin of oils to their carcinogenicity, but prefer rather to await the results of further confirmatory experiments before we give expression to opinions which we at present hold with a considerable degree of confidence.* We have, however, no hesitation in expressing our views on the oils as a whole. If a non-carcinogenic oil is required, we feel secure in recommending saponifiable oils; if a mineral oil is stipulated, then we have little difficulty in recommending that the oils should be as far as possible saturated, preferably blended with a saponifiable oil, if other conditions allow of such a blend being used.

It may be objected that although our experiments have been fairly numerous, the actual number of malignant tumors induced by the oil applications is, after all, not very great. We are willing to admit that this is so, but in addition to some 200 experiments with tars it must be understood that we have far more data on oils to go upon than are given in this abridged communication. Many of these oils have been distilled, or fractionated with methyl sulphate, methyl sulphite, picric acid, and alcohol, and animal tests with these fractions have given us much additional information. Suitable fractionation of an oil, hardly capable itself of inducing the formation of an insignificant papilloma, may lead to the production of a fraction which will induce malignant tumors with relative ease. Again, to the uninitiated it is perhaps not easy to assign the true significance to so-called benign tumors; but we are in a more fortunate position, having followed the details of the change of a benign tumor to malignancy in several thousand animals. Our potency figures have been carefully calculated; they are unfortunately only very approximate, but we ourselves are satisfied that they give us a fairly good indication of the relative ability of the agents tested to induce cancer in individuals exposed to them. The cumulative tumor figures are instructive; but for correlation purposes they are unwieldy.

In several of our previous publications we have said that in our opinion the active constituents in mineral oils and tars are probably of the nature of unsaturated benzenoid hydrocarbons. At any rate our experiments point strongly in this direction; and, on the whole, it is the saturated oils that have proved to be the least active. We shall of course not be surprised if the tumors obtained from the application of further oil samples at present under test do not run parallel with previous samples, but in this case we shall expect a corresponding difference in the degree of unsaturation of the oils. In other words, we feel confident that saturation is an important factor, but we are not so confident that the country of origin, except possibly

painted with oils 7, 11, 59, and 63, the final potencies being 8, 2, 30, and 30, respectively.

in one or two cases, is of much significance. Mineral oils of course may undergo changes during storage; but we are not at present prepared to say whether the carcinogenicity is thereby increased or decreased. It is not improbable that much will be found to depend upon the nature of the oil under consideration.

In conclusion we should like to express our thanks for materials and much help relating to technical processes utilized in the refining of oils to: Messrs. Fine Cotton Spinners Association, Messrs. James Hurst of Manchester, Messrs. O'Brien of Altrincham, Messrs. Spurrier Glazebrook of Manchester, Messrs. Anglo-Persian, Shell-Mex, Anglo-American and R. O. P. Oil Companies.

Summary

1. Potency is a measure of the response of mice to carcinogenic agents. It is a function of time.

2. Refined Scotch shale lubricating oil was in every instance found to be more potent than any refined petroleum-well oil tested.

3. In the process of manufacture of refined shale oil, the most potent fraction tested was found to be the unfinished lubricating oil. The refined oil was somewhat less potent, while the cruder products were on an average about 60 per cent. less potent.

4. The potency of crude shale oil did not appear to decrease appreciably until the retorting temperature fell below 400°C.

5. Samples of refined petroleum lubricating oils obtained from various fields of the world had widely different degrees of activity. A sample of Venezuelan oil was very potent, while Russian and Pennsylvanian samples were on an average less than one-tenth as active. Many other oils had an intermediate activity. However, two oils from the same area may have widely different activity, probably having come from different fields or having been more thoroughly refined with acid. For example, two Texas oils gave us potencies of 1 and 30, respectively

6. As a rule the heavier grade oils tested were found to be less potent than spindle oils. The amount of acid used in refining may account for the difference.

7. The addition of lanolin or sperm oil materially lessened the carcinogenic activity of the oils; in two cases 10 per cent. lanolin reduced the potency 89 per cent.

8. Several saponifiable oils tested showed no carcinogenic activity; with regard to mineral oils, it appears that in general terms, the more saturated were the constituent hydrocarbons the less capable were they of inducing cancer in our experimental animals, the physical characteristics being similar.

9. The fluorescence of oils may be related to their potency. We have examined chrysene and found that although very little soluble in the diluents used, it had a definite carcinogenic activity.

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NOTE ON THE DETERMINATION OF SMALL AMOUNTS OF BENZENE VAPORS IN AIR*

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IN 1929 the author published a method for the determination of small amounts of benzene vapors in air.[1] Results were included of a series of tests of the method, made upon known amounts of benzene vaporized into air, both alone and in the presence of various possible interferences. For pure benzene vapors the method was shown to be from 93.1 per cent. correct at 11,000 parts per million of benzene to 99.2 per cent. at 200 parts per million. In the presence of toluene the method was from 86.2 per cent. to 99 per cent. correct in determining the amount of benzene present, when there was not more than three times as much toluene as benzene in the air sample.

Since its publication in 1929 the method has been used frequently, and it has become advisable to determine its accuracy at concentrations lower than the 200 parts per million of benzene reported before. Accordingly the work briefly reported upon here has been performed.

The procedure was exactly as described before, and for all details the original paper should be consulted. In barest outline, the method consisted in catching the benzene vapors in a mixture of sulphuric and nitric acids, neutralizing, separating the dinitrobenzene formed in the acids by steam distillation (from a buffered solution when toluene was present in the air), and then titrating the nitro compound with titanous chloride. Since it was desired to prepare and test concentrations of vapors as low as 30 parts per million of benzene, it was necessary to take larger samples of air for analysis than formerly, so as to obtain enough nitrobenzene for the titration. The materials vaporized for this series of tests were the same specimens used before, and had been preserved sealed in ampoules since 1929.

Consideration of the errors possible in reading the various instrument scales involved in these determinations showed that the results have an uncertainty of about 1 per cent. of their values. Accordingly, the results are reported only to the nearest whole percentage, except in the case of pure toluene vapors, for which the nearest tenth of a per cent. is reported.

The two tables give all the data found. Table 1 shows that the method is from 99 to 100 per cent. correct with pure benzene vapors at concentrations of from 30 to 585 parts per million, and that in the presence of

* Received for publication April 14, 1931.

[1] Smyth, H. F., Jr.: The Determination of Small Amounts of Benzene Vapors in Air. THIS JOUR., 1929, *11*, 338.

various aliphatic alcohols and acetates it is just as accurate at concentrations of from 10 to 250 parts per million. The results previously published carry the concentrations above 200 parts per million. Table 2 shows that in the presence of toluene the method is from 85 to 95 per cent. correct for the benzene present for concentrations of 30 to 380 parts per million of benzene, when there is not more than three times as much toluene as benzene. When about eight times as much toluene as benzene is present, the results are considerably above 100 per cent. for the benzene present because the distillation from the buffered solution does not remove all the interference of the toluene. With pure toluene, however, only about 1 per cent. is reported as benzene. The original paper gives a little more discussion of these relations.

The results with pure benzene and with benzene in the presence of aliphatic compounds completely confirm those already published; the results with toluene are from 1 to 2 per cent.

TABLE 1.—ACCURACY OF THE METHOD FOR THE ESTIMATION OF BENZENE, IN THE ABSENCE OF TOLUENE

MATERIAL VAPORIZED	BENZENE IN AIR SAMPLE	APPROXIMATE VOLUME OF AIR SAMPLE	APPROXIMATE CONCENTRATION OF BENZENE IN SAMPLE	BENZENE FOUND BY TITRATION	ACCURACY OF RESULT
	mg.	*l.*	*p.p.m.*	*mg.*	%
Pure benzene	0.97	10.0	30	0.97	100
	1.10	10.0	35	1.09	99
	2.23	10.0	70	2.22	99
	2.25	10.0	70	2.23	99
	2.89	10.0	90	2.87	99
	3.14	6.5	150	3.13	99
	3.35	6.5	160	3.35	100
	3.96	3.0	415	3.93	99
	3.74	2.0	585	3.72	99
5.18% benzene in ethyl alcohol	0.94	30.0	10	0.93	99
	1.02	20.0	15	1.01	99
	0.95	10.0	30	0.94	99
	2.11	9.0	75	2.11	100
	3.19	10.0	100	3.18	99
	4.79	10.0	150	4.76	99
	2.49	3.5	225	2.46	99
4.99% benzene in mixture of equal parts ethyl, butyl, and amyl alcohols and acetates	0.96	20.0	15	0.95	99
	0.95	10.0	30	0.95	100
	2.30	10.0	75	2.28	99
	3.20	10.0	100	3.17	99
	4.81	10.0	150	4.78	99
	4.00	5.0	250	3.97	99

lower than those previously published. This difference is thought to be due to benzene, while the present results are based upon concentrations of one-

TABLE 2.—ACCURACY OF THE METHOD FOR THE ESTIMATION OF BENZENE, USING THE MODIFICATIONS RECOMMENDED FOR USE IN THE PRESENCE OF TOLUENE

MATERIAL VAPORIZED	BENZENE IN AIR SAMPLE	APPROXIMATE VOLUME OF AIR SAMPLE	APPROXIMATE CONCENTRATION OF BENZENE IN SAMPLE	BENZENE FOUND BY TITRATION	ACCURACY OF RESULT
	mg.	*l.*	*p.p.m.*	*mg.*	%
Pure benzene	1.01	10	30	0.98	97
	2.25	10	70	2.20	98
	3.19	10	100	3.07	96
	4.84	5	300	4.79	99
93.98% benzene in toluene	1.36	10	40	1.28	94
	3.62	10	110	3.44	95
	5.46	10	170	5.13	94
	6.10	5	380	5.80	95
63.52% benzene in toluene	1.01	10	30	0.93	92
	1.99	10	60	1.85	93
	4.62	10	145	4.24	92
	6.08	5	380	5.60	92
51.84% benzene in toluene	0.96	10	30	0.85	88
	3.22	10	100	2.74	85
	6.07	5	380	5.28	87
25.31% benzene in toluene	0.99	10	30	0.87	88
	1.60	10	50	1.36	85
	3.20	10	100	2.85	89
	4.81	5	300	4.28	89
11.12% benzene in toluene	1.00	10	30	1.30	130
	2.26	10	70	2.87	127
	3.17	10	100	3.80	120
	4.83	5	300	6.04	125
Pure toluene	0.81[1]	10	30[1]	0.01	1.2[1]
	1.59[1]	10	60[1]	0.01	0.6[1]
	2.40[1]	10	180[1]	0.02	0.8[1]
	4.02[1]	5	300[1]	0.04	1.0[1]

[1] Toluene.

the fact that the previous results were obtained with vapor concentrations of about 2,000 parts per million of tenth as much or less. Possibly the entirely empirical conditions for the removal of the interference of toluene

are not quite suited to these low concentrations of nitro compounds. It is clear from the results in Table 2 that the unknown reaction responsible for this removal of toluene varies slightly with different ratios of benzene to toluene, and it is reasonable to expect that it also varies with different concentrations of total nitro compounds.

Summary

Results are given of determinations of the accuracy of the previously published method for the determination of benzene vapors in air. The present paper shows the method to be satisfactory for determining benzene concentrations in air as low as 30 parts per million, even in the presence of such vapors as aliphatic alcohols and acetates. In the presence of not more than three times as much toluene as benzene, the method will estimate the benzene present down to a concentration of 30 parts per million, with an accuracy of over 85 per cent.

BOOK REVIEWS

FOOD ANALYSIS. TYPICAL METHODS AND THE INTERPRETATION OF RESULTS. By *A. G. Woodman*, Associate Professor of Chemistry of Foods, Massachusetts Institute of Technology. Third edition. Cloth. Pp. xii, 557 with index. International Chemical Series. New York and London: McGraw-Hill Book Co., Inc., 1931.

In this third edition of "Food Analysis," Woodman has incorporated chiefly newer methods of analysis that have the sanction of the Association of Official Agricultural Chemists and analytic data which have appeared within the past seven years. This applies also to the section on alcoholic foods, concerning which the author stated in his preface to the second edition: "For reasons which are perhaps sufficiently obvious, the portions of the book relating specifically to alcoholic beverages have been left untouched."

Needless to say, the third edition of this excellent manual is a welcome addition to the few really good books on food analysis. It possesses the unique advantage of giving information without prolixity; yet the information is always adequate. Alternate methods are given wherever possible, and the advantages and applicability of each method are carefully discussed.

The principal divisions of the book include general methods of physical and chemical determination; microscopic examination of foods (comprising a succinct account of apparatus, mounting, and photomicrographic methods, and abundantly illustrated with photomicrographs); food colors and preservatives; milk and cream; edible fats and oils; carbohydrate foods; cocoa and chocolate; spices; vinegars; flavoring extracts; and alcoholic foods. This brief listing, however, gives but an inadequate idea of the thoroughness with which the author has covered the field of food analysis.

In view of the growing importance of metals both as normal constituents and as contaminating substances from the handling or processing of food it is to be hoped that a future edition will include a chapter on the analysis of foods for their metallic content. This is, however, in no sense a criticism of the present edition. Woodman's "Food Analysis" has an insured and important place in the literature of the subject.—*Lawrence T. Fairhall.*

PREVENTIVE MANAGEMENT: MENTAL HYGIENE IN INDUSTRY. Edited by *Henry B. Elkind*, M.D.; with a Foreword by *Henry P. Kendall*, President, The Kendall Company. Cloth. Pp. xiii, 234 with index. New York: B. C. Forbes Publishing Co., 1931.

"Preventive Management" is a symposium comprising eight lectures which set forth cogent views upon the correction of faults of business management. The systems of ideas represented are mainly those of students of industrial relations and students of psychiatry. The picturesque and suggestive title given to the book was originally the subject of one of the lectures of the series.

These several contributions, with all their interesting variety of approach, evidence also a noticeable unity in the view that effective business management demands a new degree of recognition and understanding of individuality. An understanding application of the principles of these contributions cannot fail to prevent some of the conspicuous defects of the older modes of business management.

Some of the obvious defects and failings of today's business, however, are practically untouched by the preventive suggestions of these lectures. It would seem that the scientific prevention of some of these more recently recognized defects, the consequences of which weigh so heavily upon us at the present moment, is already calling for even more discriminating understanding of the needs of individuality in the midst of its industrial setting of today. —*Harold W. Stevens.*

BOOKS RECEIVED

Books received are acknowledged in this column, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers and as space permits.

PERSONAL HYGIENE FOR NURSES. By *Seneca Egbert*, A.M., M.D., Dr. P. H., Professor of Hygiene, University of Pennsylvania; Formerly Professor of Hygiene and Dean of the Medico-Chirurgical College of Philadelphia, and Professor of Anatomy and Physiology in Temple University; Lecturer at Schools of Nursing of the Graduate Hospital of the University of Pennsylvania and the Philadelphia General Hospital. Cloth. Pp. 347 with index and illustrations. Philadelphia: F. A. Davis Co., 1930.

TREATMENT OF EPILEPSY. By *Fritz B. Talbot*, M.D., Clinical Professor of Pediatrics, Harvard University Medical School; Chief of Children's Medical Department, Massachusetts General Hospital. Cloth. Pp. 308 with bibliography and index. New York: The Macmillan Co., 1930.